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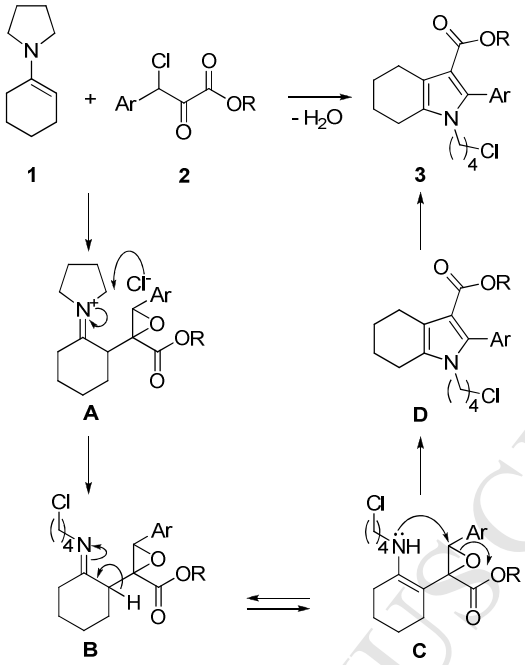
ABSTRACT: Sequential substitution/ring cleavage/addition reaction of 1-(cyclohex-1-enyl)-piperidine and -pyrrolidine with chloropyruvates has been accomplished for the synthesis of various polysubstituted 4,5,6,7-tetrahydroindoles. This one-pot, general and highly regioselective method avoids harsh conditions and expensive catalysts. It proceeds with high atom-efficiency and shows a broad substrate scope and functional group tolerance, making it a highly practical approach for the preparation of various tetrahydroindole derivatives. A family of 17 tetrahydroindoles was synthesized in good yields, which is indicative of the general character of this reaction. Ten of the tetrahydroindole derivatives with various substituents were successfully transformed into the corresponding indoles. This methodology allows access to indoles bearing ω-halo- (mostly chloro-)butyl and pentyl substituents at the nitrogen atom (by variation of enamines) and at the C2, C3 positions (by variation of pyruvates, including bromoaryl and chloroalkyl derivatives). The reaction can be used in conjunction with enamine synthesis offering a practical three-component heteroannulation methodology to produce 4,5,6,7-tetrahydroindoles from cyclohexanone, pyrrolidine and arylchloropyruvates.

KEYWORDS: Synthetic methods; Enamines; Chloropyruvates; Ring cleavage; 4,5,6,7-Tetrahydro-1*H*-indoles

INTRODUCTION

Recent studies on the chemistry of indole derivatives have focused on the development of efficient and convenient methods for the synthesis of natural products and their analogues possessing potent biological and physiological activities.[1] One of the urgent directions in this field is the creation of new pathways leading to substances possessing the 4,5,6,7-tetrahydro-1*H*-indole scaffold. This structural motif is present in two members (Tuberostemonine, Stenine) of the *Stemona* alkaloid family[2] and in two members (Lysergic acid, Isolysergic acid) of the ergot alkaloid family.[3] Besides, tetrahydroindole derivatives display a wide spectrum of biological activities: anti-implantation, hypoglycemic, anti-inflammatory, and analgesic;[4] potent neuroleptic[5] (e.g., molindone); and antitumor.[6] Tetrahydroindoles are also valuable intermediates in the synthesis of natural alkaloids[7] such as goniomitine, arcyriacyanin A, 6,7-secoagroclavine, and chuangxinmycin, as well as synthetic drugs[8] (pindolol) and highly functionalized indoles.[9] The great majority of procedures employed in construction of both *N*-substituted and *N*-unnsubstituted tetrahydroindoles are based on metal-catalyzed cyclization strategies.[10] However, the synthesis of highly functionalized pyrroles remains challenging and often requires multiple steps or harsh reaction conditions. Here the course of our ongoing research toward the synthesis of heterocycles via Darzens condensation products,[11] we describe a novel approach to the synthesis of 2,3-fused pyrroles, mainly 1,2,3-substituted 4,5,6,7-tetrahydro-1*H*-indole derivatives, via the sequential substitution/ring cleavage/addition reaction of commercially available 1-(cyclohex-1-enyl)-piperidines and 1-(cyclohex-1-enyl)-pyrrolidine with arylchloropyruvates, which are readily derived from methyl dichloroacetate and corresponding aldehydes under Darzens condensation (eq 1). We further extend this methodology to the formation of substituted indoles from 4,5,6,7-tetrahydro-1*H*-indoles.

On the basis of the new ring formation in the reactions of 1-cyclohexenylpyrrolidine **1** with arylchloropyruvates **2** we have recently developed a highly efficient and one-step versatile method for the synthesis of 4,5,6,7-tetrahydro-2-phenyl-1*H*-indole derivatives **3** bearing a 1-chlorobutyl substituent at the nitrogen atom.[12] It is based on cascade conversions involving: (a) an intramolecular nucleophilic substitution of the S_N2 type with the formation of an epoxide ring and elimination of Cl^-, (b) the opening of the pyrrolidine ring in **A** on exposure to Cl^-, (c) imino-enamine tautomerism **B** $\rightleftharpoons$ **C**, (d) the opening of the epoxide ring with a concomitant formation of the new pyrrole ring, **D**, and (e) the elimination of water leading to the formation of tetrahydroindole derivatives **3** (Scheme 1), previously reported by us.[12] According to this procedure, we obtained 1-(4-chlorobutyl)-2-(4-aryl)-3-methoxycarbonyl-4,5,6,7-tetrahydroindoles (**3**, 8 examples) in 72-90% yields (Scheme 1).



Scheme 1. Our previous work.

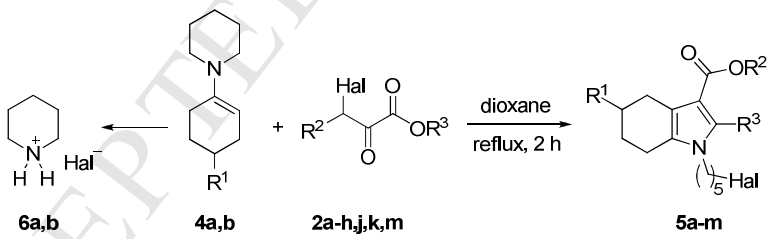
RESULTS AND DISCUSSION

We have suggested that this procedure could be applied to the synthesis of *N*-alkyltetrahydroindoles **5** (Table 1) and functionalized indoles **10** (Table 2). With this idea in mind, in order to identify the optimal reaction conditions 1-cyclohexenylpiperidine **4a** and methyl phenylchloropyruvate **2a** were chosen as the test substrates and parameters including the solvent, temperature, and molar ratio of the reagent and substrate were examined in detail. Among the solvents investigated which included ethanol, acetonitrile, dichloromethane, and dioxane, the best result in terms of yield was obtained with dioxane. The reaction was also tried at different temperatures. At room temperature, the reaction of 1-cyclohexenylpiperidine **4a** and methyl phenylchloropyruvate **2a**, depending on the reaction time gave a corresponding 4,5,6,7-tetrahydroindole derivative **5a**, piperidinium chloride **6a** and unchanged starting substrates as a mixture. When the ratio of substrates differs than 1:1, the yield of piperidinium chloride **6a** as a by product increased. Surprisingly, raising the temperature led to the formation of the 4,5,6,7-tetrahydroindole derivative **5a**, almost as a sole product in a 64% yield. However, a trace amount of piperidinium chloride **6a** was also obtained. The formation of **6a**, might occur through a piperidinium intermediate type of **A**, as a result of hydrolysis with the formation of piperidine and its hydro chlorination. The highest yield (98%) of product **5a** was obtained at reflux temperature with the ratio of substrates 1:1 for 2 h.

The scope of this protocol was then investigated under optimized reaction conditions. Substituted 3-arylhalogenopyruvates **2a-j** were subjected to the reaction with 1-(cyclohex-1-enyl)-piperidine **4a** under metal-free conditions in dioxane under reflux conditions (Table 1). In the cases of substrates with halogen atoms in the aryl group of **2** the yields of the desired products depend on the positions of atoms in the Periodic Table. The higher the position of the atom in the group, the higher the yields of 4,5,6,7-tetrahydroindole derivatives **5** and vice-versa, the lower the position of the atom in the group, the lower the yields of compounds **5**. The substrate with an electron-donating group led to decreased reaction rates (entry 11). This can be rationalized by considering the fact that these groups decrease the positive charge at the C-3 carbon atom bearing a chlorine atom. The presence of stronger electron-donating groups led to even longer reaction times. In contrast, an electron-withdrawing group (entries 7,8,9,10) accelerated the reaction. The reactions proceed successfully wiht both 1-(4-*tert*-butylcyclohex-1-enyl)-piperidine (entry 9) as an enamine component and methyl 3-bromo-2-oxo-3-phenylpropanoate as a ketone component (entry 10). This affords the corresponding products in good yields (Table 1). On the whole, substrates with an electron-withdrawing functional group formed better yields (Table 1, entries 7,8,9,10) than the electron-donating ones (Table 2, entries 5,11).

Table 1

Synthesis of methyl 1-(5-halopentyl)-2-aryl-4,5,6,7-tetrahydroindole-3-carboxylates **5**



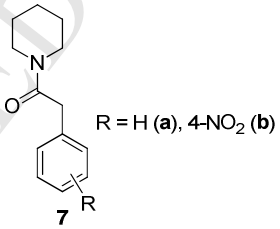
Entry	**2**	R^2	R^3	Hal	**4**	R^1	R_f[a]	Products **5:6**, yields, %
1	**2a**	C_6H_5	CH_3	Cl	**4a**	H	0.53	**5a:6a** 95:1
2	**2b**	C_6H_4Cl-4	CH_3	Cl	**4a**	H	0.51	**5b:6a** 75:12
3	**2c**	C_6H_4Br-4	CH_3	Cl	**4a**	H	0.73	**5c:6a** 71:20
4	**2d**	C_6H_4F-4	CH_3	Cl	**4a**	H	0.59	**5d:6a** 68:12
5	**2e**	C_6H_4I-4	CH_3	Cl	**4a**	H	0.59	**5e:6a** 63:22
6	**2f**	C_6H_4Br-3	CH_3	Cl	**4a**	H	0.53	**5f:6a** 76:18
7	**2g**	$C_6H_4NO_2$-4	CH_3	Cl	**4a**	H	0.46	**5g:6a** 76:14
8	**2h**	$C_6H_4NO_2$-3	CH_3	Cl	**4a**	H	0.48	**5h:6a** 80:15

9	**2d**	C_6H_4F-4	CH_3	Cl	**4b**	*t*-Bu	0.53	**5i:6a** 82:11
10	**2j**	C_6H_4F-4	C_2H_5	Br	**4a**	H	0.61	**5j:6b** 78:12
11	**2k**	C_6H_{13}	CH_3	Cl	**4a**	H	0.60	**5k:6a** 68:14
12	**2a**	C_6H_5	CH_3	Cl	**4b**	*t*-Bu	0.60	**5l:6a** 79:15
13	**2m**	C_6H_5	C_2H_5	Br	**4a**	H	0.50	**5m:6b** 66:22

[a]eluent 1:2=EtOAc:hexane

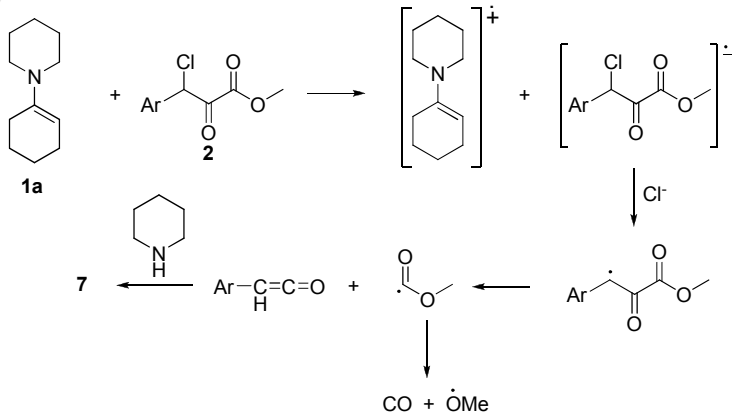
The mechanism of the formation of tetrhydroindole derivatives **5** in these reactions is clearly, similar to the mechanism of the formation of 4,5,6,7-tetrahydroindoles **3** in the reactions of 1-(1-pyrrolidino)cyclohexane **1** with arylchloropyruvates **2**.

As can be seen from the data shown in the table, the yield of the desired products for the most cases do not exceed 80% regardless of the nature of the substituent in the phenyl ring of the pyruvate derivative. To clear up the reasons above, in four cases, namely in the cases of the reactions of pyruvates **2a**,**g** and enamine **4a**, we have carefully analyzed the reaction mixture and found that in addition to the main products **5a**,**g** and the hydrochloride of piperidine **6a**, 2-aryl-1-(piperidin-1-yl)ethanones **7a**,**b** were formed as by-products.



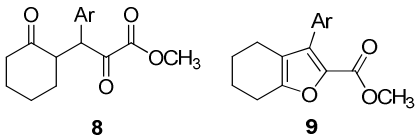
7

Although the mechanism of the formation of the products **7a**,**b** is but not as yet fully clear, we assume that under the reaction conditions there can occur side reactions involving single-electron transfer, and the formation of the products **7** can be presented as follows.



Scheme 2. Plausible mechanism of the formation of 2-aryl-1-(piperidin-1-yl)ethanones **7**.

The analysis of reaction mixtures shows that the expected products of the Stork reaction, i.e. methyl 3-aryl-2-oxo-3-(2-oxocyclohexyl)propanoates **8** or possible products of their further transformation – methyl 3-aryl-4,5,6,7-tetrahydrobenzofuran-2-carboxylates **9** – are not formed.



The structures of all compounds were established unambiguously by various 1D/2D NMR correlation methods.[13] For example, for **5k** first the proton spin systems of indole (Ind), substituents at N_1 and C_2 fragments were revealed from 1D TOCSY experiments (SI). Then, a whole structure of these moieties were established by combination of ^{1}H-^{13}C HSQC/HMBC correlations. Finally these structural fragments were "bonded" in a single whole according to ^{1}H-^{13}C/^{1}H-^{15}N HMBC connectivities (Figure 1). In addition, a number of NOEs strongly supports these structural hypotheses.

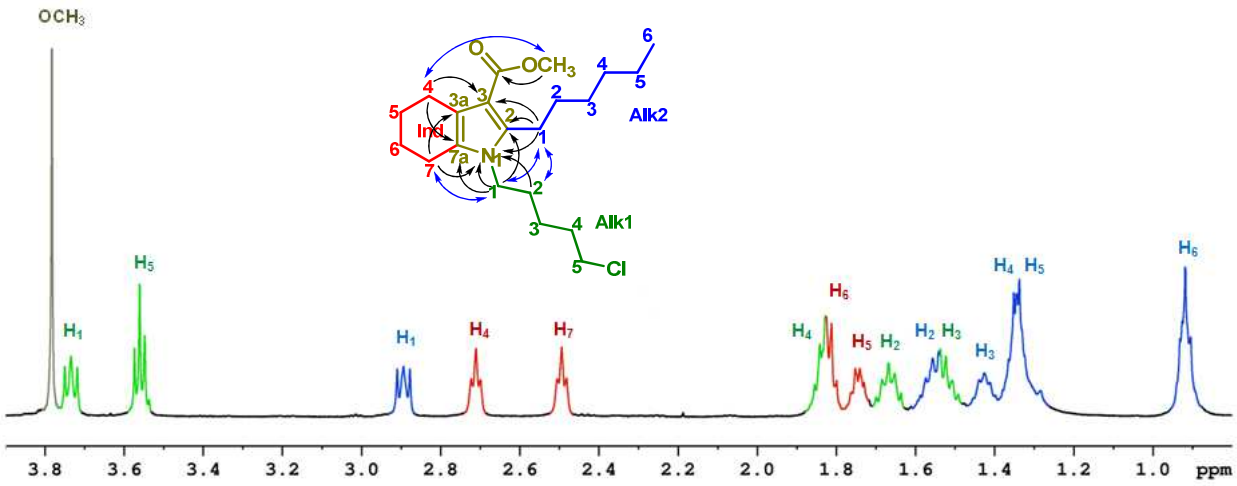


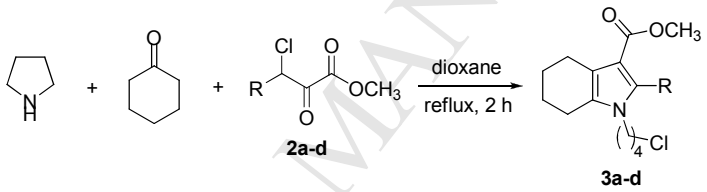
Figure 1. ^{1}H NMR spectra, structure of **5k** with principal NMR correlations (^{1}H-^{13}C and ^{1}H-^{15}N HMBC - black arrow, NOEs - blue arrow).

Assuming that enamines **4a**,**b** can be generated from the corresponding cyclohexanone derivative and piperidine, we tried to synthesize 4,5,6,7-tetrahydroindoles **5** in a three-component system "piperidine – cyclohexanone – arylchloropyruvate" in boiling dioxane. Regardless of the order of mixing the reagents and temperature conditions of the reaction, the desired products have not been

obtained, apparently due to a set of competing processes. However, the replacement of piperidine on pyrrolidine in the three-component system dramatically affects the result. The 4,5,6,7-tetrahydroindole derivatives **3** with chlorobutyl substituents in position 1 are formed with almost quantitative yields. Indeed, a test reaction between pyrrolidine and cyclohexanone in benzene, rapidly produced enamine **4a**, which underwent a sequential substitution/ring cleavage/addition reaction with arylchloropyruvate **2a** to give 4,5,6,7-tetrahydroindole **3a** with high yield (Table 2). Several arylchloropyruvates with phenyl and *para*-substituted phenyl groups **2a-d** tested reacted with similar facility, affording the corresponding products **3a-d** with high isolated yields. Further studies of the scope of this novel three-component heteroannulation reaction are underway in our laboratory.

Table 2

Synthesis of methyl 1-(5-halopentyl)-2-aryl-4,5,6,7-tetrahydroindole-3-carboxylates **3** under the three-component "pyrrolidine – cyclohexanone – arylchloropyruvate" system



2a-d **3a-d**

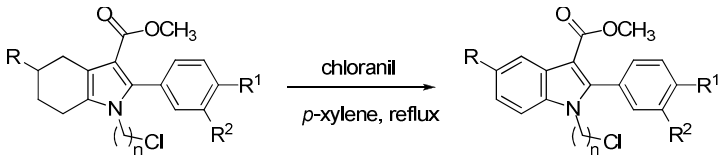
№	**2**	R	R_f[a]	Yield **3**, **%**
1	**2a**	C_6H_5	0.53	**3a**, 98
2	**2b**	C_6H_4Cl-4	0.51	**3b**, 82
3	**2c**	C_6H_4Br-4	0.73	**3c**, 88
4	**2d**	C_6H_4F-4	0.59	**3d**, 92

[a]eluent 1:2=EtOAc:hexane

Having obtained 4,5,6,7-tetrahydroindole derivatives **3** and **5** the next stage was the synthesis of the indole derivatives **10**. Dehydrogenation of **3**,**5** with the use of chloranil (in boiling *p*-xylene, 17 h) resulted in compounds **10** in good to high yields (Table 2).

Table 2

Synthesis of functionalized indole derivatives **10** from methyl 1-[5-halobutyl(and halopentyl)]-2-aryl-4,5,6,7-tetrahydroindole-3-carboxylates **3** and **5**



3 (n=4)
5 (n=5)

10a,c,d,g (n=4)
11b-d,f,g,i (n=5)

№	**3 or 5**	R^1	R^2	R	n	R_f [a]	**10**, %
1	**3a**	H	H	H	4	0.40	**10a** (85)
2	**3c**	Br	H	H	4	0.63	**10c** (82)
3	**3d**	F	H	H	4	0.51	**10d** (86)
4	**3g**	NO_2	H	H	4	0.50	**10g** (92)
5	**5b**	Cl	H	H	5	0.56	**11b** (71)
6	**5c**	Br	H	H	5	0.58	**11c** (69)
7	**5d**	F	H	H	5	0.56	**11d** (75)
8	**5f**	H	Br	H	5	0.51	**11f** (66)
9	**5g**	NO_2	H	H	5	0.48	**11g** (90)
10	**5i**	F	H	*t*-Bu	5	0.58	**11i** (78)

[a]eluent 1:2=EtOAc:hexane

CONCLUSIONS

We have developed a convenient and general approach to polysubstituted 4,5,6,7-tetrahydroindoles via the sequential substitution/ring cleavage/addition reaction between 1-cyclohexenylpiperidines and 1-cyclohexenylpyrrolidine and pyruvates. This reaction was successfully combined with the enamine synthesis, which led to the development of an efficient sequential three-component heteroannulation methodology for the construction of the methyl 1-(4-chlorobutyl)-2-aryl-4,5,6,7-tetrahydro-1*H*-indole-3-carboxylates. Dehydrogenation of 4,5,6,7-tetrahydroindole derivatives with chloranil provides an easy access to the poly-functionalized indole scaffold. Studies aimed at the extensionof this reaction to other heterocycles are presently underway in our laboratory.

EXPERIMENTAL SECTION

4. Experimental

4.1. General

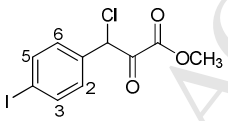
All NMR experiments were performed with 600, 500 and 400 MHz (600, 500 and 400 MHz for ^{1}H NMR; 470 and 376 MHz for ^{19}F NMR; 150, 125 and 100 MHz for ^{13}C NMR; 60 and 50.7 MHz for

^{15}N NMR, respectively) spectrometers equipped with a 5 mm diameter gradient inverse broad band probehead and a pulsed gradient unit capable of producing magnetic field pulse gradients in the z-direction of 53.5 G·cm^{-1}. NMR experiments were carried out at 303 K. DPFGROE[14] and TOCSY spectra were obtained using a Hermite-shaped pulse for selective excitation. Chemical shifts (δ in ppm) are referenced to the solvents ($CDCl_3$ (δ = 7.27 ppm for ^{1}H and 77.0 ppm for ^{13}C NMR) or DMSO-d_6 (δ = 2.49 ppm for ^{1}H and 39.5 ppm for ^{13}C NMR), to external CD_3NO_2 (380.2 ppm) for ^{15}N NMR spectra (conversion factor to NH_3: -380.2 ppm) and to external C_6F_6 (-164.9 ppm) for ^{19}F NMR spectra. The melting points were determined on a Boetius hot-stage apparatus and are uncorrected. Infrared (IR) spectra were recorded on a Bruker Vector-22 spectrometer. Mass spectra of MALDI were measured on a Bruker mass spectrometer UltraFlex III TOF/TOF. As the matrices 2,5-dihydroxybenzoic acid and *para*-nitroaniline were used. For the accurate mass measuring PEG-400 was used. The insertion of the sample was performed with direct injection combined with a water cooling system. The elemental analyses were carried out at the microanalysis laboratory of the Arbuzov Institute of Organic and Physical Chemistry, Russian Academy of Sciences. All solvents were of regent grade and were dried and distilled before use.

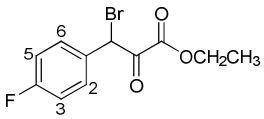
4.2. Preparation of 3-chloro(or bromo)-2-oxo-3-arylpropanoates 2

The starting compounds **2a**,[11a] **2b**,[11b] **2c**,[11c] **2d**,[11d] **2f**,[11e] **2g**,[11b] **2h**,[11f] **2k**,[11g] and **2m**,[11a] were prepared according to the published procedures.

Methyl 3-chloro-3-(4-iodophenyl)-2-oxopropanoate (2e) was prepared from methyl 2,2-dichloroacetate and *p*-iodobenzaldehyde in toluene using the method described for the synthesis of **2m**.[11b] Yellow oil; yield (72%) **2e**; ν_{max}(thin film) 1738, 1590, 1489, 1440, 1245, 1165, 856, 750 cm^{-1}. δ_H (400 MHz, $CDCl_3$) 3.84 (3 H, s, OCH_3), 6.08 (1 H, s, CH), 7.15 (2 H, d, *J* 8.4 Hz, H3,5-Ar), 7.73 (2 H, d, *J* 8.4 Hz, H2,6-Ar).



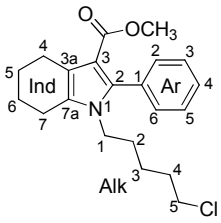
Ethyl 3-bromo-3-(4-fluorophenyl)-2-oxopropanoate (2j) was prepared from ethyl 2,2-dibromoacetate and *p*-fluorobenzaldehyde in toluene using the method described for the synthesis of **2m**.[11b] Yellow oil; yield 2.17 g (85%) **2j**; ν_{max}(thin film) 1736, 1605, 1510, 1300, 1231, 1160, 1055, 856, 839 cm^{-1}. δ_H (500 MHz, $CDCl_3$) 1.33 (3 H, t, *J* 7.1 Hz, $OCH_2\underline{CH_3}$), 4.33 (2 H, q, *J* 7.1 Hz, $O\underline{CH_2}CH_3$), 6.19 (1 H, s, CH), 7.06 (2H, dd, J_{HH} 8.6 Hz, J_{HF} 8.6 Hz, H2,6-Ar), 7.45 (2 H, dd, J_{HH} 8.6 Hz, J_{HF} 3.3 Hz, H3,5-Ar).



4.3. General procedure for the synthesis of 5.

A mixture of alkyl 3-chloro(or bromo)-2-oxo-3-arylpropanoate **1** (3.0 mmol), 1-cyclohexenylpiperidine (or 4-*tert*-butyl-1-cyclohexenylpiperidine) **4a**(**b**) (5.2 mmol) and dioxane (30 mL) was heated at reflux for 2 h. After cooling down to room temperature, the precipitate was filtered and recrystallized in toluene (or washed with *i*-PrOH) to give piperidinium chloride (or bromide) **6**. The solvent was removed to give a slightly brown crude product **5**, which was purified on column chromatography with silica gel (eluent – hexane/EtOAc).

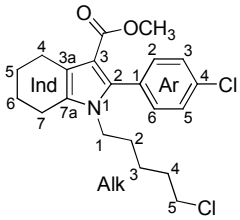
Methyl 1-(5-chloropentyl)-2-phenyl-4,5,6,7-tetrahydro-1H-indole-3-carboxylate 5a.



Colorless oil; yield 1.03 g, 95% (**5a**); 3.7 mg, 1% (**6a**); R_f (hexane/EtOAc 2:1) 0.53; [Found: C, 69.9; H, 7.3; N, 3.8. $C_{21}H_{26}ClNO_2$ requires C, 70.08; H, 7.28; Cl, 9.85; N, 3.89]. ν_{max}(thin film) 3061, 3026, 2937, 2853, 1697, 1606, 1580, 1525, 1481, 1443, 1407, 1373, 1331, 1270, 1238, 1204, 1154, 1121, 1091, 1053, 1025, 963, 919, 845, 825, 786, 763, 733, 703, 648, 612, 516 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.21-1.27 (2 H, m, CH_2-Alk3), 1.46-1.52 (2 H, m, CH_2-Alk2), 1.54-1.60 (2 H, m, CH_2-Alk4), 1.80-1.81 (2 H, m, CH_2-Ind5), 1.87-1.88 (2 H, m, CH_2-Ind6), 2.56-2.59 (2 H, m, CH_2-Ind7), 2.79-2.82 (2 H, m, CH_2-Ind4), 3.38 (2 H, t, *J* 6.6 Hz, CH_2-Alk5), 3.57 (3 H, s, OCH_3), 3.64 (2 H, t, *J* 7.6 Hz, CH_2-Alk1), 7.31-7.33 (2 H, m, H2,H6-Ar), 7.38-7.46 (3 H, m, H3,H4,H5-Ar). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 165.6 (C=O), 137.2 (C2-Ind), 132.7 (C1-Ar), 130.4 (C2-Ar), 128.0 (C7a-Ind), 127.7 (C4-Ar), 127.6 (C3-Ar), 118.8 (C3a-Ind), 110.3 (C3-Ind), 49.9 (O<u>CH</u>$_3$), 44.2 (C5-Alk), 43.1 (C1-Alk), 31.4 (C4-Alk), 29.7 (C2-Alk), 23.5 (C3-Alk), 23.2 (C5-Ind), 23.2 (C4-Ind), 22.8 (C6-Ind), 22.0 (C7-Ind). ^{15}N NMR (50.6 MHz, $CDCl_3$): δ 164.9 (N1). HRMS (MALDI) calcd. for $C_{21}H_{26}ClNO_2$ $[M+Cs]^+$ 492,0701, found 492,0718.

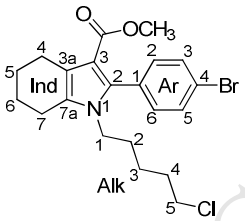
Tetrahydroindoles **5b-k** were obtained in a similar way from appropriate chloropyruvates.[11]

Methyl 1-(5-chloropentyl)-2-(4-chlorophenyl)-4,5,6,7-tetrahydro-1H-indole-3-carboxylate 5b.



Pale yellow oil; yield 0.89 g, 75% (**5b**); 43 mg, 12% (**6a**); R_f (hexane/EtOAc 2:1) 0.51; [Found: C, 63.9; H, 6.5; N, 3.4. $C_{21}H_{25}Cl_2NO_2$ requires C, 63.96; H, 6.39; Cl, 17.98; N, 3.55]. ν_{max}(thin film) 2928, 2853, 1702, 1601, 1523, 1480, 1442, 1410, 1374, 1331, 1269, 1237, 1204, 1154, 1122, 1091, 1015, 965, 824, 785, 755, 734, 650, 612, 507 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.24-1.30 (2 H, m, CH_2-Alk3), 1.44-1.50 (2 H, m, CH_2-Alk2), 1.58-1.64 (2 H, m, CH_2-Alk4), 1.76-1.81 (2 H, m, CH_2-Ind5), 1.84-1.89 (2 H, m, CH_2-Ind6), 2.55 (2 H, br t, *J* 6.0 Hz, CH_2-Ind7), 2.77 (2 H, br t, *J* 6.1 Hz, CH_2-Ind4), 3.42 (2 H, t, *J* 6.6 Hz, CH_2-Alk5), 3.59 (3 H, s, OCH_3), 3.61 (2 H, t, *J* 7.8 Hz, CH_2-Alk1), 7.25 (2H, d, *J* 8.5 Hz, H3,H5-Ar), 7.39 (2H, d, *J* 8.5 Hz, H2,H6-Ar). $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$): δ 165.8 (C=O), 136.0 (C2-Ind), 134.1 (C4-Ar), 132.1 (C2-Ar), 131.4 (C1-Ar), 128.7 (C7a-Ind), 128.2 (C3-Ar), 119.3 (C3a-Ind), 111.0 (C3-Ind), 50.3 (OCH_3), 44.4 (C5-Alk), 43.5 (C1-Alk), 31.8 (C4-Alk), 30.1 (C2-Alk), 23.9 (C3-Alk), 23.4 (C5-Ind +C4-Ind), 23.0 (C6-Ind), 22.3 (C7-Ind). ^{15}N NMR (50.6 MHz, $CDCl_3$): δ 164.6 (N1).

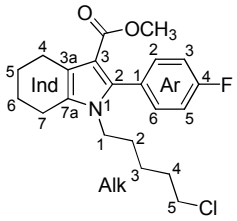
Methyl 2-(4-bromophenyl)-1-(5-chloropentyl)-4,5,6,7-tetrahydro-1H-indole-3-carboxylate 5c.



Yellow oil; yield 0.93 g, 71% (**5c**); 72 mg, 20% (**6a**); R_f (hexane/EtOAc 2:1) 0.73; [Found: C, 57.4; H, 5.9; N, 3.0. $C_{21}H_{25}BrClNO_2$ requires C, 57.48; H, 5.74; Br, 18.21; Cl, 8.08; N, 3.19]. ν_{max}(thin film) 2938, 2853, 1697, 1521, 1479, 1442, 1410, 1270, 1204, 1122, 1073, 1011, 822, 785, 755, 735, 650, 502 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.22-1.28 (2H, m, CH_2-Alk3), 1.44-1.50 (2H, m, CH_2-Alk2), 1.58-1.64 (2H, m, CH_2-Alk4), 1.76-1.81 (2H, m, CH_2-Ind5), 1.84-1.89 (2H, m, CH_2-Ind6), 2.55 (2H, br t, *J* 6.0 Hz, CH_2-Ind7), 2.76 (2H, br t, *J* 6.1 Hz, CH_2-Ind4), 3.42 (2H, t, *J* 6.6 Hz, CH_2-Alk5), 3.59 (3H, s, OCH_3), 3.61 (2H, t, *J* 7.7 Hz, CH_2-Alk1), 7.18 (2H, d, *J* 8.4 Hz, H3,H5-Ar), 7.54 (2H, d, *J* 8.4 Hz, H2,H6-Ar). $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$): δ 165.8 (C=O), 136.0 (C2-Ind), 132.4 (C2-

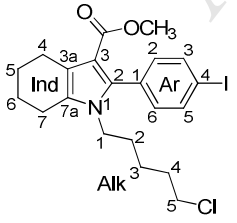
Ar), 131.9 (C1-Ar), 131.1 (C3-Ar), 128.7 (C7a-Ind), 122.4 (C4-Ar), 119.3 (C3a-Ind), 111.0 (C3-Ind), 50.3 (CO$\underline{CH_3}$), 44.4 (C5-Alk), 43.5 (C1-Alk), 31.8 (C4-Alk), 30.1 (C2-Alk), 23.8 (C3-Alk), 23.4 (C4-Ind+C5-Ind), 23.0 (C6-Ind), 22.2 (C7-Ind).

Methyl 1-(5-chloropentyl)-2-(4-fluorophenyl)-4,5,6,7-tetrahydro-1H-indole-3-carboxylate 5d.



Maize yellow oil; yield 0.77 g, 68% (**5d**); 43 mg, 12% (**6a**); R_f (hexane/EtOAc 2:1) 0.59; [Found: C, 66.5; H, 6.4; N, 3.7. $C_{21}H_{25}ClFNO_2$ requires C, 66.75; H, 6.67; Cl, 9.38; F, 5.03; N, 3.71]. ν_{max}(thin film) 2929, 2854, 1702, 1606, 1535, 1489, 1460, 1442, 1412, 1374, 1331, 1269, 1223, 1204, 1156, 1121, 1092, 1016, 965, 833, 821, 787, 735, 651, 591, 523 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.23-1.29 (2H, m, CH_2-Alk3), 1.44-1.50 (2H, m, CH_2-Alk2), 1.57-1.63 (2H, m, CH_2-Alk4), 1.77-1.81 (2H, m, CH_2-Ind5), 1.85-1.89 (2H, m, CH_2-Ind6), 2.55 (2H, br t, *J* 6.2 Hz, CH_2-Ind7), 2.77 (2H, br t, *J* 6.1 Hz, CH_2-Ind4), 3.41 (2H, t, *J* 6.6 Hz, CH_2-Alk5), 3.59 (3H, s, OCH_3), 3.61 (2H, br t, *J* 7.8 Hz, CH_2-Alk1), 7.11 (2H, dd, J_{HH} 8.7 Hz, J_{HF} 8.7 Hz, H2,H6-Ar), 7.28 (2H, dd, J_{HH} 8.7 Hz, J_{HF} 3.0 Hz, H3,H5-Ar). $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$): δ 165.8 (C=O), 162.5 (d, $^1J_{CF}$ = 247.5 Hz, C4-Ar), 136.3 (C2-Ind), 132.5 (d, $^3J_{CF}$ = 8.2 Hz, C2-Ar), 128.9 (d, $^4J_{CF}$ = 3.6 Hz, C1-Ar), 128.4 (C7a-Ind), 119.2 (C3a-Ind), 115.0 (d, $^2J_{CF}$ = 21.5 Hz, C3-Ar), 110.9 (C3-Ind), 50.3 (O$\underline{CH_3}$), 44.4 (C5-Alk), 43.4 (C1-Alk), 31.8 (C4-Alk), 30.1 (C2-Alk), 23.9 (C3-Alk), 23.4 (C4-Ind+C5-Ind), 23.1 (C6-Ind), 22.2 (C7-Ind). $^{19}F\{^1H\}$ NMR (470.5 MHz, $CDCl_3$): δ 113.7 (F).

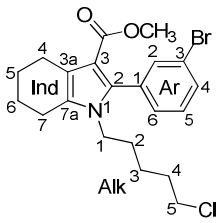
Methyl 1-(5-chloropentyl)-2-(4-iodophenyl)-4,5,6,7-tetrahydro-1H-indole-3-carboxylate 5e.



Yellow oil; yield 0.92 g, 63% (**5e**); 79 mg, 22% (**6a**); R_f (hexane/EtOAc 2:1) 0.59; [Found: C, 52.3; H, 5.3; N, 2.7. $C_{21}H_{25}ClINO_2$ requires C, 51.92; H, 5.19; Cl, 7.30; I, 26.12; N, 2.88]. ν_{max} (thin film)

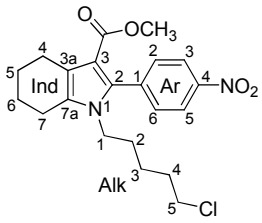
2924, 2853, 1702, 1582, 1519, 1475, 1461, 1409, 1376, 1317, 1261, 1238, 1204, 1184, 1154, 1121, 1092, 1023, 1007, 966, 817, 799, 752, 734, 648, 613 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.25-1.31 (2H, m, CH_2-Alk3), 1.46-1.52 (2H, m, CH_2-Alk2), 1.60-1.66 (2H, m, CH_2-Alk4), 1.79-1.82 (2H, m, CH_2-Ind5), 1.86-1.90 (2H, m, CH_2-Ind6), 2.57 (2H, br t, *J* 5.7 Hz, CH_2-Ind7), 2.78 (2H, br t, *J* 6.1 Hz, CH_2-Ind4), 3.44 (2H, t, *J* 6.6 Hz, CH_2-Alk5), 3.62 (3H, s, OCH_3), 3.63 (2H, t, *J* 7.7 Hz, CH_2-Alk1), 7.07 (2H, d, *J* 8.3 Hz, H3,H5-Ar), 7.77 (2H, d, *J* 8.3 Hz, H2,H6-Ar). $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$): δ 165.8 (C=O), 137.1 (C3-Ar), 136.1 (C2-Ind), 132.6 (C2-Ar), 132.5 (C1-Ar), 128.7 (C7a-Ind), 119.4 (C3a-Ind), 111.0 (C3-Ind), 94.2 (C 4-Ar), 50.4 ($O\underline{CH_3}$), 44.5 (C5-Alk), 43.5 (C1-Alk), 31.8 (C4-Alk), 30.1 (C2-Alk), 23.9 (C3-Alk), 23.4 (C5-Ind+C4-Ind), 23.0 (C6-Ind), 22.3 (C-Ind).

Methyl 2-(3-bromophenyl)-1-(5-chloropentyl)-4,5,6,7-tetrahydro-1H-indole-3-carboxylate 5f.



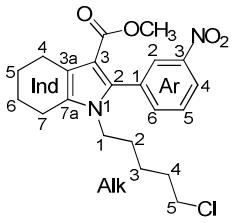
Pale yellow oil; yield 1.00 g, 76% (**5f**); 65 mg, 18% (**6a**); R_f (hexane/EtOAc 2:1) 0.53; [Found: C, 57.2; H, 5.8; N, 3.1. $C_{21}H_{25}BrClNO_2$ requires C, 57.48; H, 5.74; Br, 18.21; Cl, 8.08; N, 3.19]. ν_{max} (thin film) 2927, 2854, 1703, 1600, 1579, 1561, 1520, 1471, 1441, 1409, 1374, 1330, 1320, 1269, 1238, 1204, 1154, 1122, 1092, 1051, 1030, 997, 964, 890, 784, 755, 714, 700, 652, 535, 437 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.24-1.30 (2H, m, CH_2-Alk3), 1.45-1.51 (2H, m, CH_2-Alk2), 1.58-1.64 (2H, m, CH_2-Alk4), 1.76-1.80 (2H, m, CH_2-Ind5), 1.85-1.89 (2H, m, CH_2-Ind6), 2.55 (2H, br t, *J* 6.1 Hz, CH_2-Ind7), 2.77 (2H, br t, *J* 6.1 Hz, CH_2-Ind4), 3.42 (2H, t, *J* 6.6 Hz, CH_2-Alk5), 3.59 (3H, s, OCH_3), 3.62 (2H, t, *J* 7.7 Hz, CH_2-Alk1), 7.26 (1H, ddd, *J* 7.6 Hz, 1.6, 1.6 Hz, H6-Ar), 7.29 (1H, dd, *J* 7.6, 7.6 Hz, H5-Ar), 7.47 (1H, dd, *J* 1.6, 1.6 Hz, H2-Ar), 7.52 (1H, ddd, *J* 7.6, 1.6, 1.6 Hz, H4-Ar). $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$): δ 165.7 (C=O), 135.5 (C2-Ind), 135.0 (C1-Ar), 133.6 (C2-Ar), 131.0 (C4-Ar), 129.6 (C5-Ar), 129.3 (C6-Ar), 128.8 (C7a-Ind), 121.7 (C3-Ar), 119.4 (C3a-Ind), 111.1 (C3-Ind), 50.3 (OCH_3), 44.4 (C5-Alk), 43.5 (C1-Alk), 31.7 (C4-Alk), 30.1 (C2-Alk), 23.8 (C3-Alk), 23.4 (C5-Ind), 23.3 (C4-Ind), 23.0 (C6-Ind), 22.2 (C7-Ind).

Methyl 1-(5-chloropentyl)-2-(4-nitrophenyl)-4,5,6,7-tetrahydro-1H-indole-3-carboxylate 5g.



Yellow oil; yield 0.92 g, 76% (**5g**); 50 mg, 14% (**6a**); R_f (hexane/EtOAc 2:1) 0.46; [Found: C, 62.0; H, 6.4; N, 6.7. $C_{21}H_{25}ClN_2O_4$ requires C, 62.30; H, 6.22; Cl, 8.76; N, 6.92]. ν_{max} (thin film) 2954, 2925, 2854, 1702, 1601, 1579, 1521, 1462, 1414, 1377, 1345, 1261, 1205, 1155, 1122, 1107, 1092, 1047, 1016, 967, 863, 853, 803, 755, 721, 708, 648 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.23-1.29 (2H, m, CH_2-Alk3), 1.43-1.49 (2H, m, CH_2-Alk2), 1.57-1.63 (2H, m, CH_2-Alk4), 1.77-1.82 (2H, m, CH_2-Ind5), 1.86-1.90 (2H, m, CH_2-Ind6), 2.57 (2H, br t, *J* 6.1 Hz, CH_2-Ind7), 2.77 (2H, br t, *J* 6.1 Hz, CH_2-Ind4), 3.41 (2H, t, *J* 6.5 Hz, CH_2-Alk5), 3.60 (3H, s, OCH_3), 3.65 (2H, t, *J* 7.8 Hz, CH_2-Alk1), 7.50 (2H, d, *J* 8.8 Hz, H3,H5-Ar), 8.28 (2H, d, *J* 8.8 Hz, H2,H6-Ar). $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$): δ 165.5 (C=O), 147.4 (C4-Ar), 139.9 (C1-Ar), 134.5 (C2-Ind), 131.8 (C2-Ar), 129.8 (C7a-Ind), 123.1 (C3-Ar), 119.9 (C3a-Ind), 111.8 (C3-Ind), 50.5 (OCH_3), 44.4 (C5-Alk), 43.7 (C1-Alk), 31.7 (C4-Alk), 30.1 (C2-Alk), 23.8 (C3-Alk), 23.3 (C4-Ind), 23.3 (C5-Ind), 23.0 (C6-Ind), 22.3 (C7-Ind).

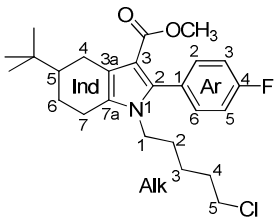
Methyl 1-(5-chloropentyl)-2-(3-nitrophenyl)-4,5,6,7-tetrahydro-1H-indole-3-carboxylate 5h.



Yellow oil; yield 0.97 g, 80% (**5h**); 54 mg, 15% (**6a**); R_f (hexane/EtOAc 2:1) 0.48; [Found: C, 62.0; H, 6.4; N, 6.8. $C_{21}H_{25}ClN_2O_4$ requires C, 62.30; H, 6.22; Cl, 8.76; N, 6.92]. ν_{max} (thin film) 2926, 2854, 1702, 1619, 1579, 1536, 1519, 1474, 1442, 1407, 1349, 1265, 1238, 1206, 1155, 1126, 1098, 1054, 1025, 965, 908, 858, 807, 787, 739, 711, 697, 651 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.22-1.28 (2H, m, CH_2-Alk3), 1.46-1.52 (2H, m, CH_2-Alk2), 1.57-1.63 (2H, m, CH_2-Alk4), 1.76-1.82 (2H, m, CH_2-Ind5), 1.86-1.90 (2H, m, CH_2-Ind6), 2.57 (2H, br t, *J* 6.0 Hz, CH_2-Ind7), 2.77 (2H, br t, *J* 6.0 Hz, CH_2-Ind4), 3.41 (2H, t, *J* 6.5 Hz, CH_2-Alk5), 3.59 (3H, s, OCH_3), 3.64 (2H, t, *J* 7.7 Hz, CH_2-Alk1), 7.60 (1H, br dd, *J* 7.6, 7.6 Hz, H5-Ar), 7.68 (1H, br d, *J* 7.6 Hz, H6-Ar), 8.20 (1H, d, *J* 1.3 Hz, H2-Ar), 8.26 (1H, dd, *J* 7.6, 1.3 Hz, H4-Ar). $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$): δ 165.5 (C=O), 147.9 (C3-Ar), 137.2 (C6-Ar), 134.6 (C1-Ar), 134.3 (C2-Ind), 129.4 (C7a-Ind), 128.8 (C5-Ar), 125.6 (C2-Ar),

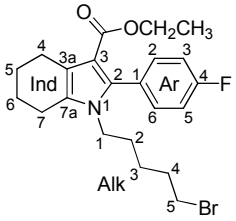
122.9 (C4-Ar), 119.7 (C3a-Ind), 111.7 (C3-Ind), 50.5 (OCH_3), 44.4 (C5-Alk), 43.6 (C1-Alk), 31.9 (C4-Alk), 30.2 (C2-Alk), 23.9 (C3-Alk), 23.3 (C4-Ind), 23.3 (C5-Ind), 23.0 (C6-Ind), 22.2 (C7-Ind). HRMS (MALDI) calcd. for $C_{21}H_{25}ClN_2O_4$ $[M + Cs]^+$ 537.0552, found 537.0528.

Methyl 5-tert-butyl-1-(5-chloropentyl)-2-(4-fluorophenyl)-4,5,6,7-tetrahydro-1H-indole-3-carboxylate 5i.



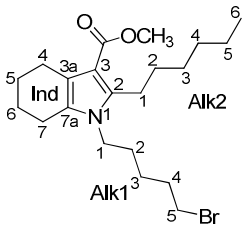
Maize yellow oil; yield 1.07 g, 82% (**5i**); 40 mg, 11% (**6a**); R_f (hexane/EtOAc 2:1) 0.65; [Found: C, 61.9; H, 6.3; N, 6.6. $C_{25}H_{33}ClFNO_2$ requires C, 62.30; H, 6.22; Cl, 8.76; N, 6.92]. ν_{max} (thin film) 2953, 2868, 1702, 1658, 1604, 1536, 1508, 1488, 1468, 1413, 1396, 1366, 1310, 1224, 1158, 1125, 1095, 1073, 1058, 1015, 918, 838, 788, 753, 733, 651, 620, 591, 524 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.00 (9H, s, $(CH_3)_3$), 1.22-1.28 (2H, m, CH_2-Alk3), 1.39-1.50 (4H, m, CH_2-Alk2, CH_X-Ind5, CH_A-Ind6), 1.56-1.62 (2H, m, CH_2-Alk4), 2.06-2.11 (1H, m, CH_B-Ind6), 2.37-2.41 (1H, m, CH_A-Ind4), 2.49-2.55 (1H, m, CH_A-Ind7), 2.64-2.68 (1H, m, CH_B-Ind7), 2.96-3.01 (1H, m, CH_B-Ind4), 3.40 (2H, t, *J* 6.5 Hz, CH_2-Alk5), 3.57 (3H, s, OCH_3), 3.60 (2H, t, *J* 7.7 Hz, CH_2-Alk1), 7.09 (2H, dd, J_{HH} 8.8 Hz, J_{HF} 8.8 Hz, H2,H6-Ar), 7.27 (2H, dd, J_{HH} 8.8 Hz, J_{HF} 3.4 Hz, H3,H5-Ar). $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): δ 165.8 (C=O), 162.5 (d, $^1J_{CF}$ = 247.6 Hz, C4-Ar), 136.4 (C2-Ind), 132.4 (d, $^3J_{CF}$ = 8.2 Hz, C2-Ar), 128.9 (d, $^4J_{CF}$ = 3.3 Hz, C1-Ar), 128.6 (C7a-Ind), 119.6 (C3a-Ind), 114.9 (d, $^2J_{CF}$ = 21.6 Hz, C3-Ar), 110.9 (C3-Ind), 50.2 (OCH_3), 45.3 (C5-Ind), 44.4 (C5-Alk), 43.5 (C1-Alk), 32.5 (C-$(CH_3)_3$), 31.7 (C4-Alk), 30.0 (C2-Alk), 27.4 (C-$(CH_3)_3$), 24.6 (C4-Ind), 24.5 (C6-Ind), 23.8 (C3-Alk), 23.1 (C7-Ind). $^{19}F\{^1H\}$ NMR (376.5 MHz, $CDCl_3$): δ 113.5 (F).

Ethyl 1-(5-bromopentyl)-2-(4-fluorophenyl)-4,5,6,7-tetrahydro-1H-indole-3-carboxylate 5j.



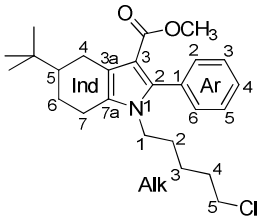
Yellow oil; yield 1.02 g, 78% (**5j**); 60 mg, 12% (**6a**); R_f (hexane/EtOAc 2:1) 0.60; [Found: C, 60.1; H, 6.4; N, 3.0. $C_{22}H_{27}BrFNO_2$ requires C, 60.55; H, 6.24; Br, 18.31; F, 4.35; N, 3.21]. ν_{max} (thin film) 2936, 2857, 1732, 1697, 1600, 1509, 1489, 1459, 1414, 1255, 1158, 1117, 1094, 1038, 838, 523 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.06 (3H, t, *J* 7.1, $OCH_2\underline{CH_3}$), 1.22-1.28 (2H, m, CH_2-Alk3), 1.44-1.50 (2H, m, CH_2-Alk2), 1.65-1.71 (2H, m, CH_2-Alk4), 1.77-1.81 (2H, m, CH_2-Ind5), 1.85-1.89 (2H, m, CH_2-Ind6)**,** 2.55 (2H, br t, *J* 5.9 Hz, CH_2-Ind7), 2.78 (2H, br t, *J* 5.9 Hz, CH_2-Ind4), 3.28 (2H, t, *J* 6.6 Hz, CH_2-Alk5), 3.60 (2H, t, *J* 7.7 Hz, CH_2-Alk1), 4.04 (2H, q, *J* 7.1 Hz, $O\underline{CH_2}CH_3$), 7.10 (2H, dd, J_{HH} 8.6 Hz, J_{HF} 8.6 Hz, H2,H6-Ar), 7.28 (2H, dd, J_{HH} 8.6 Hz, J_{HF} 3.0 Hz, H3,H5-Ar). $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$): δ 165.3 (C=O), 162.5 (d, $^1J_{CF}$ = 247.1 Hz, C4-Ar), 136.1 (C2-Ind), 132.5 (d, $^3J_{CF}$ = 8.2 Hz, C2-Ar), 129.0 (d, $^2J_{CF}$ = 3.4 Hz, C1-Ar), 128.4 (C7a-Ind), 119.2 (C3a-Ind), 114.9 (d, $^2J_{CF}$ = 21.6 Hz, C3-Ar), 111.2 (C3-Ind), 58.8 ($O\underline{C}H_2CH_3$), 43.4 (C1-Alk), 33.1 (C5-Alk), 31.8 (C4-Alk), 29.9 (C2-Alk), 25.1 (C3-Alk), 23.4 (C5-Ind), 23.3 (C4-Ind), 23.0 (C6-Ind), 22.2 (C7-Ind), 14.1 ($OCH_2\underline{C}H_3$). $^{19}F\{^1H\}$ NMR (470.5 MHz, $CDCl_3$): δ -113.8 (F).

Methyl 1-(5-chloropentyl)-2-hexyl-4,5,6,7-tetrahydro-1H-indole-3-carboxylate 5k.



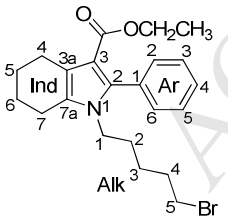
Colorless oil; yield 0.75 g, 68% (**5j**); 50 mg, 14% (**6a**); R_f (hexane/EtOAc 2:1) 0.60; [Found: C, 68.4; H, 9.6; N, 3.6. $C_{21}H_{24}ClNO_2$ requires C, 68.55; H, 9.31; Cl, 9.64; N, 3.81]. ν_{max} (thin film) 2931, 2856, 1695, 1518, 1441, 1422, 1328, 1259, 1237, 1187, 1155, 1113, 1032, 786, 732, 653 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ_H 0.89 (3H, t, *J* 6.8 Hz, CH_2-Alk2-6), 1.26-1.34 (4H, m, CH_2-Alk2-4, CH_2-Alk2-5), 1.37-1.43 (2H, m, CH_2-Alk2-3), 1.47-1.56 (4H, m, CH_2-Alk2-2, CH_2-Alk1-3), 1.61-1.67 (2H, m, CH_2-Alk1-2), 1.71-1.74 (2H, m, CH_2-Ind5), 1.77-1.83 (4H, m, CH_2-Ind6, CH_2-Alk1-4), 2.47 (2H, br t, *J* 5.8 Hz, CH_2-Ind7), 2.68 (2H, br t, *J* 5.9 Hz, CH_2-Ind4), 2.87 (2H, br t, *J* 8.0 Hz, CH_2-Alk2-1), 3.54 (2H, t, *J* 6.5 Hz, CH_2-Alk1-5), 3.71 (2H, t, *J* 7.8 Hz, CH_2-Alk1-1), 3.76 (3H, s, OCH_3). $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$): δ 166.4 (C=O), 139.4 (C2-Ind), 126.9 (C7a-Ind), 118.5 (C3a-Ind), 108.6 (C3-Ind), 50.1 (OCH_3), 44.5 (C5-Alk1), 42.9 (C1-Alk1), 32.1 (C4-Alk1), 31.6 (C4-Alk2), 30.6 (C2-Alk1), 30.5 (C2-Alk2), 29.5 (C3-Alk2), 25.5 (C1-Alk2), 24.2 (C3-Alk1), 23.5 (C4-Ind+C5-Ind), 23.1 (C6-Ind), 22.6 (C5-Alk2), 22.1 (C7-Ind), 14.0 (C6-Alk2). ^{15}N NMR (50.6 MHz, $CDCl_3$): δ 163.7 (N). HRMS (MALDI) calcd. for $C_{21}H_{34}ClNO_2$ $[M+Cs]^+$ 500.1327, found 500.1354.

Methyl 5-tert-butyl-1-(5-chloropentyl)-2-phenyl-4,5,6,7-tetrahydro-1H-indole-3-carboxylate 5l.



Maize yellow oil; yield 0.99 g, 79% (**5l**); 54 mg, 15% (**6a**); R_f (hexane/EtOAc 2:1) 0.60; [Found: C, 71.9; H, 8.5; N, 3.2. $C_{25}H_{34}ClNO_2$ requires C, 72.18; H, 8.24; Cl, 8.52; N, 3.37]. ν_{max} (thin film) 2953, 2926, 2855, 1703, 1480, 1444, 1407, 1366, 1310, 1207, 1165, 1124, 1098, 761, 702 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.00 (9H, s, $(CH_3)_3$), 1.22-1.30 (2H, m, CH_2-Alk3), 1.42-1.51 (4H, m, CH_2-Alk2, CH_X-Ind5, CH_A-Ind6), 1.55-1.60 (2H, m, CH_2-Alk4), 2.09-2.12 (1H, m, CH_B-Ind6), 2.40-2.43 (1H, m, CH_A-Ind4), 2.51-2.54 (1H, m, CH_A-Ind7), 2.65-2.68 (1H, m, CH_B-Ind7), 3.00-3.03 (1H, m, CH_B-Ind4), 3.39 (2H, t, *J* 6.6 Hz, CH_2-Alk5), 3.57 (3H, s, OCH_3), 3.63 (2H, t, *J* 7.7 Hz, CH_2-Alk1), 7.31 (2H, dd, *J* 8.0, 1.7 Hz, H2,H6-Ar), 7.38-7.43 (3H, m, H3,H4,H5-Ar). $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$): δ 165.9 (C=O), 137.7 (C2-Ind), 133.0 (C1-Ar), 130.7 (C2-Ar), 128.4 (C7a-Ind), 127.9 (C4-Ar), 127.8 (C3-Ar), 119.6 (C3a-Ind), 110.6 (C3-Ind), 50.2 (OCH_3), 45.4 (C5-Ind), 44.4 (C5-Alk), 43.5 (C1-Alk), 32.5 ($\underline{C}(CH_3)_3$), 31.7 (C4-Alk), 30.0 (C2-Alk), 27.5 ($C(\underline{C}H_3)_3$), 24.7 (C4-Ind), 24.5 (C6-Ind), 23.8 (C3-Alk), 23.1 (C7-Ind). HRMS (MALDI) calcd. for $C_{25}H_{34}ClNO_2$ $[M+Cs]^+$ 548.1327, found 548.1320.

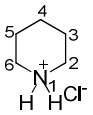
Ethyl 1-(5-bromopentyl)-2-phenyl-4,5,6,7-tetrahydro-1H-indole-3-carboxylate 5m.



Yellow oil; yield 0.83 g, 66% (**5l**); 0.11 g, 22% (**6a**); R_f (hexane/EtOAc 2:1) 0.50; [Found: C, 63.0; H, 7.0; N, 3.2. $C_{25}H_{34}ClNO_2$ requires C, 63.16; H, 6.75; Br, 19.10; N, 3.35]. ν_{max} (thin film) 2935, 1752, 1695, 1484, 1454, 1264, 1202, 1158, 1115, 754, 700 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.00 (3H, t, *J* 7.1 Hz, $OCH_2\underline{CH_3}$), 1.23-1.27 (2H, m, CH_2-Alk3), 1.44-1.50 (2H, m, CH_2-Alk2), 1.62-1.68 (2H, m, CH_2-Alk4), 1.78-1.82 (2H, m, CH_2-Ind5), 1.85-1.90 (2H, m, CH_2-Ind6), 2.56 (2H, br t, *J* 6.1 Hz,

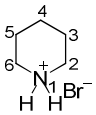
CH_2-Ind7), 2.80 (2H, br t, *J* 6.0 Hz, CH_2-Ind4), 3.25 (2H, t, *J* 6.7 Hz, CH_2-Alk5), 3.62 (2H, t, *J* 7.7 Hz, CH_2-Alk1), 4.03 (2H, q, *J* 7.1 Hz, O<u>CH_2</u>CH_3), 7.30 (2H, dd, *J* 7.9, 2.1 Hz, H2,H6-Ar), 7.37-7.40 (3H, m, H3,H4,H5-Ar). $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$): δ 165.4 (C=O), 137.4 (C2-Ind), 133.1 (C1-Ar), 130.8 (C2-Ar), 128.2 (C7a-Ind), 127.9 (C4-Ar), 127.8 (C3-Ar), 119.2 (C3a-Ind), 110.9 (C3-Ind), 58.8 (O<u>C</u>H_2CH_3), 43.4 (C1-Alk), 33.1 (C5-Alk), 31.9 (C4-Alk), 29.9 (C2-Alk), 25.1 (C3-Alk), 23.5 (C4-Ind), 23.3 (C5-Ind), 23.1 (C6-Ind), 22.3 (C7-Ind), 14.0 (OCH_2<u>C</u>H_3). ^{15}N NMR (50.6 MHz, $CDCl_3$): δ 164.4 (N).

Piperidinium chloride 6a.



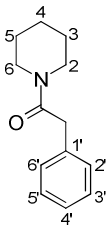
Off-white powder, m.p. 247-248 ^oC; [Found: C, 49.3; H, 10.0; N, 11.3. $C_5H_{12}ClN$: C, 49.38; H, 9.95; Cl, 29.15; N, 11.52]. ν_{max} (thin film) 2950, 2842, 2809, 2763, 2735, 2527, 2428, 1593, 1462, 1437, 1032, 943, 557 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ_H 1.51-1.57 (2H, m, CH_2-4), 1.65-1.70 (4H, m, CH_2-3,CH_2-5), 2.95 (4H, t, *J* 5.7 Hz, CH_2-2,CH_2-6), 9.15 (2H, br s, NH_2). $^{13}C\{^1H\}$ NMR (100.6 MHz, DMSO-d_6): δ 43.3 (C2, C6), 21.9 (C3, C5), 21.7 (C4). ^{15}N NMR (50.6 MHz, DMSO-d_6): δ 41.5 (N).

Piperidinium bromide 6b.



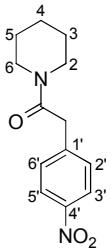
Off-white powder, m.p. 334-336 ^oC; [Found: C, 36.0; H, 7.5; N, 8.3. $C_5H_{12}BrN$: C, 36.16; H, 7.28; Br, 48.12; N, 8.43]. ν_{max} (thin film) 3177, 2949, 2840, 2808, 2738, 2627, 2513, 2413, 1586, 1462, 1434, 1030, 551 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ_H δ 1.51-1.57 (2H, m, CH_2-4), 1.63-1.68 (4H, m, CH_2-3,CH_2-5), 3.00 (4H, t, *J* 5.0 Hz, CH_2-2,CH_2-6), 8.42 (2H, br s, NH_2). $^{13}C\{^1H\}$ NMR (100.6 MHz, DMSO-d_6): δ 43.8 (C2, C6), 22.1 (C3, C5), 21.6 (C4).

2-Phenyl-1-(piperidin-1-yl)ethanone 7a.



Colorless oil; yield 24 mg, 4%; R_f (hexane/EtOAc 2:1) 0.60; [Found: C, 76.5; H, 8.6; N, 6.7. $C_{13}H_{17}NO$ requires C, 76.81; H, 8.43; N, 6.89]. ν_{max} (thin film) 3028, 3005, 2937, 2856, 1738, 1640, 1444, 1368, 1256, 1225, 1136, 1123, 1022, 726, 698 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ_H 1.29-1.33 (2H, m, CH_2-3), 1.37-1.41 (2H, m, CH_2-5), 1.51-1.55 (2H, m, CH_2-4), 3.40 (2H, t, *J* 5.6 Hz, CH_2-2), 3.43 (2H, t, *J* 5.6 Hz, CH_2-6), 3.68 (2H, s, CH_2), 7.21 (1H, t, *J* 7.4 Hz, H4′), 7.22 (2H, d, *J* 7.7 Hz, H2′, H6′), 7.30 (2H, dd, *J* 7.4, 7.7 Hz, H3′, H5′). $^{13}C\{^1H\}$ NMR (125.7 MHz, DMSO-d_6): δ 168.3 (C=O), 136.0 (C1-Ar), 128.7 (C2-Ar), 128.2 (C3-Ar), 126.2 (C4-Ar), 46.4 (C2), 42.0 (C6), 39.7 ($\underline{C}H_2$), 25.8 (C3), 25.2 (C5), 23.9 (C4). ^{15}N NMR (50.6 MHz, DMSO-d_6): δ 121.1 (N1). HRMS (MALDI) calcd. for $C_{13}H_{17}NO$ $[M+Cs]^+$ 336.0359, found 336.0330.

2-(4-nitrophenyl)-1-(piperidin-1-yl)ethanone 7b.

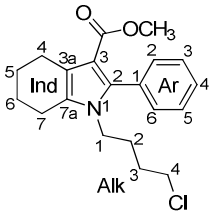


Yellow oil; yield 45 mg, 6%; R_f (hexane/EtOAc 2:1) 0.60; Found: C, 62.8; H, 6.7; N, 11.1. $C_{13}H_{16}N_2O_3$ requires C, 62.89; H, 6.50; N, 11.28. ν_{max} (thin film) 2932, 1923, 2854, 1736, 1632, 1606, 1517, 1443, 1423, 1346, 1250, 1225, 1135, 1109, 1013, 857, 820, 734 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ_H 1.44-1.46 (2H, m, CH_2-3), 1.53-1.55 (2H, m, CH_2-5), 1.60-1.63 (2H, m, CH_2-4), 3.40 (2H, t, *J* 5.3 Hz, CH_2-2), 3.58 (2H, t, *J* 5.3 Hz, CH_2-6), 3.81 (2H, s, CH_2), 7.42 (2H, d, *J* 8.8 Hz, H2′, H6′), 8.17 (2H, d, *J* 8.8 Hz, H3′, H5′). $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$): δ 167.7 (C=O), 147.0 (C4-Ar), 143.0 (C1-Ar), 129.8 (C2-Ar), 123.7 (C3-Ar), 47.2 (C2), 43.1 (C6), 40.4 (CH_2), 26.4 (C3), 25.4 (C5), 24.3 (C4). ^{15}N NMR (50.6 MHz, $CDCl_3$) δ 124.5 (N1), 370.0 (NO_2). HRMS (MALDI) calcd. for $C_{13}H_{16}N_2O_3$ $[M+Cs]^+$ 381.0210, found 381.0240.

4.4. General procedure for the synthesis of 3.

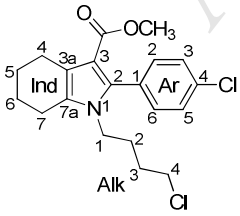
A solution of pyrrolidine (5 mmol) and cyclohexanone a (5 mmol) in benzene (25 mL) was heated to reflux with the Dean-Stark apparatus for 1 h, then cooled to room temperature and methyl 3-chloro-2-oxo-3-arylpropanoate **2** (5 mL) in benzene was added then heated to reflux for another 2 h. The solvent was removed to give a slightly yellow crude product **3**, which was purified on column chromatography with silica gel (eluent – hexane/EtOAc).

Methyl 1-(4-chlorobutyl)-2-phenyl-4,5,6,7-tetrahydro-1H-indole-3-carboxylate 3a.



Colorless oil; yield 1.69 g, 98%; R_f (hexane/EtOAc 2:1) 0.53; [Found: C, 69.1; H, 6.8; N, 3.9. $C_{20}H_{24}ClNO_2$ requires C, 69.45; H, 6.99; Cl, 10.25; N, 4.05]. ν_{max} (thin film) 2933, 2853, 1702, 1527, 1481, 1459, 1441, 1406, 1370, 1276, 1250, 1204, 1154, 1120, 1086, 1025, 757, 702 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.52-1.58 (2H, m, CH_2-Alk3), 1.58-1.64 (2H, m, CH_2-Alk2), 1.78-1.82 (2H, m, CH_2-Ind5), 1.86-1.90 (2H, m, CH_2-Ind6), 2.58 (2H, br t, *J* 6.0 Hz, CH_2-Ind7), 2.79 (2H, br t, *J* 6.1 Hz, CH_2-Ind4), 3.32 (2H, t, *J* 6.3 Hz, CH_2-Alk4), 3.58 (3H, s, OCH_3), 3.66 (2H, t, *J* 7.4 Hz, CH_2-Alk1), 7.30-7.32 (2H, m, H2,H6-Ar), 7.38-7.43 (3H, m, H3,H4,H5-Ar). $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$): δ 165.8 (C=O), 137.5 (C2-Ind), 132.8 (C1-Ind), 130.7 (C2-Ar), 128.2 (C7a-Ind), 128.0 (C4-Ar), 127.9 (C3-Ar), 119.2 (C3a-Ind), 110.7 (C3-Ind), 50.2 (OCH_3), 44.0 (C4-Alk), 42.8 (C1-Alk), 29.3 (C3-Alk), 27.9 (C2-Alk), 23.4 (C5-Ind), 23.3 (C4-Ind), 23.0 (C6-Ind), 22.2 (C7-Ind). ^{15}N NMR (50.6 MHz, $CDCl_3$): δ 163.9 (N).

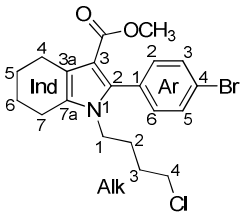
Methyl 1-(4-chlorobutyl)-2-(4-chlorophenyl)-4,5,6,7-tetrahydro-1H-indole-3-carboxylate 3b.



Maize yellow oil; yield 1.56 g, 82%; R_f (hexane/EtOAc 2:1) 0.51; [Found: C, 63.0; H, 6.3; N, 3.5. $C_{20}H_{23}Cl_2NO_2$ requires C, 63.16; H, 6.10; Cl, 18.64; N, 3.68]. ν_{max} (thin film) 2922, 2850, 1701, 1525,

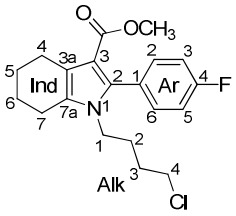
1479, 1449, 1440, 1400, 1368, 1276, 1265, 1233, 1200, 1152, 1124, 1085, 1010, 965, 824, 786, 750, 734 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.54-1.64 (4H, m, CH_2-Alk2, CH_2-Alk3), 1.76-1.82 (2H, m, CH_2-Ind5), 1.84-1.90 (2H, m, CH_2-Ind6), 2.56 (2H, br t, *J* 6.1 Hz, CH_2-Ind7), 2.77 (2H, br t, *J* 6.1 Hz, CH_2-Ind4), 3.36 (2H, t, *J* 6.2 Hz, CH_2-Alk4), 3.60 (3H, s, OCH_3), 3.65 (2H, t, *J* 7.3 Hz, CH_2-Alk1), 7.25 (2H, d, *J* 8.5 Hz, H3,H5-Ar), 7.40 (2H, d, *J* 8.5 Hz, H2,H6-Ar). $^{13}C\{^{1}H\}$ NMR (125.7 MHz, $CDCl_3$): δ 165.7 (C=O), 136.1 (C2-Ind), 134.2 (C4-Ar), 132.1 (C2-Ar), 131.3 (C1-Ar), 128.7 (C7a-Ind), 128.2 (C3-Ar), 119.4 (C3a-Ind), 111.1 (C3-Ind), 50.3 (OCH_3), 44.0 (C4-Alk), 42.9 (C1-Alk), 29.4 (C3-Alk), 28.0 (C2-Alk), 23.4 (C5-Ind+C4-Ind), 23.0 (C6-Ind), 22.3 (C7-Ind). ^{15}N NMR (50.6 MHz, $CDCl_3$): δ 163.8 (N1).

Methyl 1-(4-chlorobutyl)-2-(4-bromophenyl)-4,5,6,7-tetrahydro-1H-indole-3-carboxylate 3c.



Yellow oil; yield 1.87 g, 88%; R_f (hexane/EtOAc 2:1) 0.73; [Found: C, 56.3; H, 5.6; N, 3.2. $C_{20}H_{23}BrClNO_2$ requires C, 56.55; H, 5.46; Br, 18.81; Cl, 8.35; N, 3.30]. ν_{max} (thin film) 2935, 2853, 1699, 1520, 1480, 1440, 1406, 1266, 1274, 1210, 1204, 1128, 1120, 1075, 1021, 757, 735 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ_H 1.54-1.58 (2H, m, CH_2-Alk3), 1.59-1.63 (2H, m, CH_2-Alk2), 1.78-1.80 (2H, m, CH_2-Ind5), 1.86-1.88 (2H, m, CH_2-Ind6), 2.56 (2H, br t, *J* 6.1 Hz, CH_2-Ind7), 2.76 (2H, br t, *J* 6.1 Hz, CH_2-Ind4), 3.36 (2H, t, *J* 6.2 Hz, CH_2-Alk4), 3.59 (3H, s, OCH_3), 3.64 (2H, t, *J* 7.3 Hz, CH_2-Alk1), 7.18 (2H, d, *J* 8.4 Hz, H3,H5-Ar), 7.55 (2H, d, *J* 8.4 Hz, H2,H6-Ar). $^{13}C\{^{1}H\}$ NMR (150.9 MHz, $CDCl_3$): δ 165.7 (C=O), 136.0 (C2-Ind), 132.4 (C1-Ar), 132.4 (C2-Ar), 131.2 (C3-Ar), 128.7 (C7a-Ind), 122.4 (C4-Ar), 119.5 (C3a-Ind), 111.2 (C3-Ind), 50.3 (OCH_3), 44.0 (C4-Alk), 42.9 (C1-Alk), 29.4 (C3-Alk), 28.1 (C2-Alk), 23.4 (C4-Ind+C5-Ind), 23.1 (C6-Ind), 22.3 (C7-Ind).

Methyl 1-(4-chlorobutyl)-2-(4-fluorophenyl)-4,5,6,7-tetrahydro-1H-indole-3-carboxylate 3d.

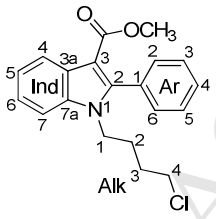


Colorless oil; yield 1.67 g, 92%; R_f (hexane/EtOAc 2:1) 0.59; [Found: C, 65.9; H, 6.6; N, 3.7. $C_{20}H_{23}ClFNO_2$ requires C, 66.02; H, 6.37; Cl, 9.74; F, 5.22; N, 3.85]. ν_{max} (thin film) 2924, 2850, 1704, 1600, 1527, 1480, 1459, 1441, 1406, 1370, 1276, 1250, 1204, 1154, 1122, 1090, 1025, 757, 732, 702, 646, 592, 521 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.55-1.61 (4H, m, CH_2-Alk2, CH_2-Alk3), 1.78-1.81 (2H, m, CH_2-Ind5), 1.85-1.88 (2H, m, CH_2-Alk6), 2.56 (2H, br t, *J* 6.0 Hz, CH_2-Ind7), 2.77 (2H, br t, *J* 6.0 Hz, CH_2-Ind4), 3.35 (2H, t, *J* 6.1 Hz, CH_2-Alk4), 3.59 (3H, s, OCH_3), 3.64 (2H, t, *J* 7.4 Hz, CH_2-Alk1), 7.11 (2H, dd, J_{HH} 8.7 Hz, J_{HF} 8.7 Hz, H2,H6-Ar), 7.28 (2H, dd, J_{HH} 8.7 Hz, J_{HF} 3.0 Hz, H3,H5-Ar). $^{13}C\{^1H\}$ NMR (125.7 MHz, $CDCl_3$): δ 165.8 (C=O), 162.6 (d, $^1J_{CF}$ 247.9 Hz, C4-Ar), 136.4 (C2-Ind), 132.5 (d, $^3J_{CF}$ 8.2 Hz, C2-Ar), 128.8 (d, $^4J_{CF}$ 3.1 Hz, C1-Ar), 128.5 (C7a-Ind), 119.3 (C3a-Ind), 115.0 (d, $^2J_{CF}$ 21.4 Hz, C3-Ar), 111.1 (C3-Ind), 50.3 (OCH_3), 44.0 (C4-Alk), 42.9 (C1-Alk), 29.7 (C3-Alk), 28.0 (C2-Alk), 23.4 (C4-Ind+C5-Ind), 23.1 (C6-Ind), 22.3 (C7-Ind). $^{19}F\{^1H\}$ NMR (470.5 MHz, $CDCl_3$): δ 113.6 (F). HRMS (MALDI) calcd. for $C_{20}H_{23}ClFNO_2$ $[M + Cs]^+$ 496.0450, found 496.0414.

General procedure for the synthesis of 10.

4.5. A solution of **3** or **5** (0.5 mmol) and 0.61 g of chloranil (2.5 mmol) in *p*-xylene (20 mL) was heated at reflux for 17 h, cooled, filtered and the solid residue was washed with ether (3×5 mL). The solvent was evaporated in vacuo and the residue was chromatographed (hexane : EtOAc) to give a pure indole derivative **10**.

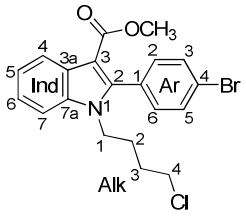
Methyl 1-(5-chloropentyl)-2-phenyl-1H-indole-3-carboxylate 10a.



Colorless oil; yield 1.45 g, 85%; R_f (hexane/EtOAc 2:1) 0.40; [Found: C, 70.1; H, 6.0; N, 3.9. $C_{20}H_{20}ClNO_2$ requires C, 70.27; H, 5.90; Cl, 10.37; F, 5.22; N, 4.10]. ν_{max} (thin film) 2951, 2927, 1694, 1541, 1483, 1460, 1406, 1234, 1190, 1146, 1117, 1092. 1026, 791, 753, 701, 646 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.48-1.54 (2H, m, CH_2-Alk3), 1.63-1.69 (2H, m, CH_2-Alk2), 3.44 (2H, t, *J* 6.5, CH_2-Alk4), 3.60 (3H, s, OCH_3), 4.05 (2H, t, *J* 7.3 Hz, CH_2-Alk1), 7.26 (1H, ddd, *J* 7.5, 7.4, 1.1 Hz, H5-Ind), 7.31 (1H, ddd, *J* 7.0, 6.8, 1.3 Hz, H6-Ind), 7.43-7.46 (2H, m, H3,H5-Ar), 7.51-7.53 (3H, m,

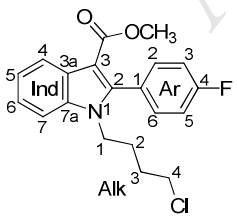
H2,H4, H6-Ar), 7.75 (1H, br d, *J* 8.2 Hz, H7-Ind), 8.09 (1H, br d, *J* 6.3 Hz, H4-Ind). $^{13}C\{^{1}H\}$ NMR (125.7 MHz, $CDCl_3$): δ 164.3 (C=O), 146.1 (C2-Ind), 135.6 (C7a-Ind), 131.0 (C1-Ar), 130.1 (C2-Ar), 128.8 (C4-Ar), 128.0 (C3-Ar), 126.0 (C3a-Ind), 122.7 (C6-Ind), 121.8 (C5-Ind), 121.2 (C4-Ind), 110.9 (C7-Ind), 104.2 (C3-Ind), 50.3 (OCH_3), 44.5 (C4-Alk), 42.6 (C1-Alk), 29.0 (C3-Alk), 26.5 (C2-Alk). ^{15}N NMR (50.6 MHz, $CDCl_3$): δ 150.8 (N1). HRMS (MALDI) calcd. for $C_{20}H_{20}ClNO_2$ $[M+Cs]^+$ 474.0232, found 474.0249.

Methyl 2-(4-bromophenyl)-1-(4-chlorobutyl)-1H-indole-3-carboxylate 10c.



Sallow oil; yield 1.72 g, 82%; R_f (hexane/EtOAc 2:1) 0.63; [Found: C, 56.9; H, 5.0; N, 3.2. $C_{20}H_{19}BrClNO_2$ requires C, 57.09; H, 4.55; Br, 18.99; Cl, 8.43; N, 3.33]. ν_{max} (thin film) 3598, 3160, 2142, 1660, 1040, 1014, 968, 889, 756, 656 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ_H 1.50-1.56 (2H, m, CH_2-Alk3), 1.62-1.68 (2H, m, CH_2-Alk2), 3.47 (2H, t, *J* 6.5 Hz, CH_2-Alk4), 3.63 (3H, s, OCH_3), 4.06 (2H, t, *J* 7.3 Hz, CH_2-Alk1), 7.26 (1H, ddd, *J* 8.1, 7.2, 1.1 Hz, H5-Ind), 7.32 (1H, ddd, *J* 8.0, 7.2, 1.3 Hz, H6-Ind), 7.41 (2H, d, *J* 8.5 Hz, H3,H5-Ar), 7.66 (1H, br d, *J* 8.0 Hz, H7-Ind), 7.72 (2H, d, *J* 8.5 Hz, H2,H6-Ar), 8.09 (1H, dd, *J* 8.0, 1.0 Hz, H4-Ind). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, DMSO-d_6): δ 164.2 (C=O), 144.7 (C2-Ind), 135.7 (C7a-Ind), 132.3 (C2-Ar), 131.0 (C3-Ar), 130.3 (C1-Ar), 125.9 (C3a-Ind), 122.8 C6-Ind), 122.5 (C4-Ar), 121.9 (C5-Ind), 121.2 (C4-Ind), 111.0 (C7-Ind), 104.5 (C3-Ind), 50.4 (OCH_3), 44.5 (C4-Alk), 42.7 (C1-Alk), 29.0 (C3-Alk), 26.5 (C2-Alk).

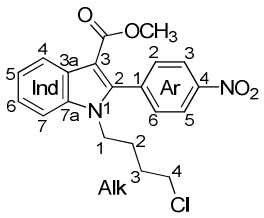
Methyl 2-(4-fluorophenyl)-1-(4-chlorobutyl)-1H-indole-3-carboxylate 10d.



Reddish-brown oil; yield 1.55 g, 86%; R_f (hexane/EtOAc 2:1) 0.51; [Found: C, 66.7; H, 5.5; N, 3.7. $C_{20}H_{19}ClFNO_2$ requires C, 66.76; H, 5.32; Cl, 9.85; F, 5.28; N, 3.89]. ν_{max} (thin film) 3580, 3176,

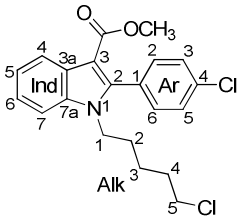
2262, 1650, 1038, 1022, 988, 860, 781, 744, 720, 662, 635 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 1.49-1.56 (2H, m, CH_2-Alk3), 1.62-1.69 (2H, m, CH_2-Alk2), 3.46 (2H, t, *J* 6.4 Hz, CH_2-Alk4), 3.62 (3H, s, OCH_3), 4.05 (2H, t, *J* 7.3 Hz, CH_2-Alk1), 7.24-7.31 (2H, m, H5,H6-Ind), 7.35 (2H, dd, J_{HH} 8.7 Hz, J_{HF} 8.7 Hz, H2,H6-Ar), 7.51 (2H, dd, J_{HH} 8.7 Hz, J_{HF} 3.0 Hz, H3,H5-Ar), 7.66 (1H, d, *J* 8.0 Hz, H7-Ind), 8.09 (1H, d, *J* 8.1 Hz, H4-Ind). $^{13}C\{^{1}H\}$ NMR (100.6 MHz, DMSO-d_6): δ 164.3 (C=O), 162.4 (d, $^{1}J_{CF}$ = 245.7 Hz, C4-Ar), 145.0 (C2-Ind), 135.7 (C7a-Ind), 132.5 (d, $^{3}J_{CF}$ 8.4 Hz, C2-Ar), 127.4 (d, $^{4}J_{CF}$ 3.2 Hz, C1-Ar), 125.9 (C3a-Ind), 122.8 (C6-Ind), 121.8 (C5-Ind), 121.2 (C4-Ind), 115.0 (d, $^{2}J_{CF}$ 21.7 Hz, C3-Ar), 111.0 (C7-Ind), 104.5 (C3-Ind), 50.4 (OCH_3), 44.5 (C4-Alk), 42.6 (C1-Alk), 29.0 (C3-Alk), 26.5 (C2-Alk). $^{19}F\{^{1}H\}$ NMR (376.5 MHz, DMSO-d_6): δ 112.6 (F). HRMS (MALDI) calcd. for $C_{20}H_{19}FClNO_2$ $[M+H]^+$ 360.1161, found 360.1132.

Methyl 2-(4-nitrophenyl)-1-(4-chlorobutyl)-1H-indole-3-carboxylate 10g.



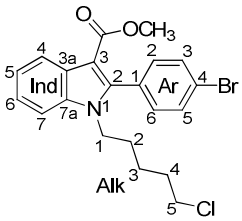
Brown oil; yield 1.78 g, 92%; R_f (hexane/EtOAc 2:1) 0.50; [Found: C, 61.9; H, 5.2; N, 7.1. $C_{20}H_{19}ClN_2O_4$ requires C, 62.10; H, 4.95; Cl, 9.17; N, 7.24]. ν_{max} (thin film) 2498, 2864, 1688, 1603, 1520, 1485, 1457, 1439, 1389, 1348, 1194, 1160, 1145, 1119, 1017, 860, 790, 754, 710 cm^{-1}. ^{1}H NMR (600 MHz, $CDCl_3$): δ_H 1.50-1.55 (2H, m, CH_2-Alk3), 1.62-1.67 (2H, m, CH_2-Alk2), 3.47 (2H, t, *J* 6.6 Hz, CH_2-Alk4), 3.63 (3H, s, OCH_3), 4.09 (2H, t, *J* 7.5 Hz, CH_2-Alk1), 7.30 (1H, dd, *J* 7.0, 7.9 Hz, H5-Ind), 7.35 (1H, ddd, *J* 7.0, 7.9, 0.9 Hz, H6-Ind), 7.71 (1H, br d, *J* 7.9 Hz, H7-Ind), 7.79 (2H, d, *J* 8.8 Hz, H2,6-Ind), 8.11 (1H, br d, *J* 7.9 Hz, H4-Ind), 8.36 (2H, d, *J* 8.8 Hz, H3,5-Ar). $^{13}C\{^{1}H\}$ NMR (150.9 MHz, DMSO-d_6): δ 164.1 (C=O), 147.7 (C4-Ar), 143.5 (C2-Ind), 138.0 (C1-Ar), 136.0 (C7a-Ind), 131.9 (C2-Ar), 125.7 (C3a-Ind), 123.1 (C6-Ind), 123.0 (C3-Ar), 122.1 (C5-Ind), 121.3 (C4-Ind), 111.1 (C7-Ind), 105.0 (C3-Ind), 50.5 (OCH_3), 44.5 (C4-Alk), 42.8 (C1-Alk), 28.9 (C3-Alk), 26.5 (C2-Alk). ^{15}N NMR (50.6 MHz, DMSO-d_6): δ 150.2 (N1), 370.4 (NO_2).

Methyl 1-(5-chloropentyl)-2-(4-chlorophenyl)-1H-indole-3-carboxylate 11b.



Maize yellow oil; yield 1.39 g, 71%; R_f (hexane/EtOAc 2:1) 0.56; [Found: C, 64.5; H, 5.5; N, 3.4. $C_{21}H_{21}Cl_2NO_2$ requires C, 64.62; H, 5.42; Cl, 18.17; N, 3.59]. ν_{max} (thin film) 3622, 3154, 2257, 2130, 1665, 1153, 1053, 1041, 1016, 979, 828, 772, 669 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ_H 1.14-1.22 (2H, m, CH_2-Alk3), 1.48-1.59 (4H, m, CH_2-Alk2, CH_2-Alk4), 4.02 (2H, t, *J* 7.5 Hz, CH_2-Alk5), 3.62 (3H, s, OCH_3), 4.02 (2H, t, *J* 7.5 Hz, CH_2-Alk1), 7.26 (1H, ddd, *J* 7.2, 7.7, 1.2 Hz, H5-Ind), 7.31 (1H, ddd, *J* 7.2, 7.9, 1.3 Hz, H6-Ind), 7.48 (2H, d, *J* 8.6 Hz, H3,H5-Ar), 7.58 (2H, d, *J* 8.6 Hz, H2,H6-Ind), 7.64 (1H, br d, *J* 7.9 Hz, H7-Ind), 8.09 (1H, dd, *J* 7.7, 1.3 Hz, H4-Ind). $^{13}C\{^1H\}$ NMR (150.9 MHz, DMSO-d_6): δ 164.3 (C=O), 144.7 (C2-Ind), 135.7 (C7a-Ind), 133.8 (C4-Ar), 132.1 (C2-Ar), 130.0 (C1-Ar), 128.1 (C3-Ar), 125.9 (C3a-Ind), 122.8 (C6-Ind), 121.8 (C5-Ind), 121.2 (C4-Ind), 111.0 (C7-Ind), 104.4 (C3-Ind), 50.4 (OCH_3), 44.9 (C5-Alk), 43.2 (C1-Alk), 31.2 (C4-Alk), 28.3 (C2-Alk), 23.3 (C3-Alk). HRMS (MALDI) calcd. for $C_{21}H_{21}Cl_2NO_2$ $[M+Cs]^+$ 521.9998, found 522.0021.

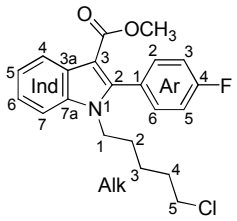
Methyl 1-(5-chloropentyl)-2-(4-bromophenyl)-1H-indole-3-carboxylate 11c.



Yellow oil; yield 1.50 g, 69%; R_f (hexane/EtOAc 2:1) 0.58; [Found: C, 57.7; H, 5.0; N, 3.1. $C_{21}H_{21}BrClNO_2$ requires C, 58.02; H, 4.87; Br, 18.38; Cl, 8.15; N, 3.22]. ν_{max} (thin film) 3603, 3175, 2257, 2130, 1666, 1649, 1041, 1014, 979, 827, 754 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.14-1.21 (2H, m, CH_2-Alk3), 1.48-1.59 (4H, m, CH_2-Alk2, CH_2-Alk4), 3.48 (2H, t, *J* 6.7 Hz, CH_2-Alk5), 3.63 (3H, s, OCH_3), 4.02 (2H, t, *J* 7.5 Hz, CH_2-Alk1), 7.26 (1H, ddd, *J* 7.6, 7.8, 1.1 Hz, H5-Ind), 7.31 (1H, ddd, *J* 7.6, 8.1, 1.3 Hz, H6-Ind), 7.42 (2H, d, *J* 8.5 Hz, H3,H5-Ar), 7.65 (1H, br d, *J* 8.1 Hz, H7-Ind), 7.72 (2H, d, *J* 8.5 Hz, H2,H6-Ar), 8.08 (1H, ddd, *J* 7.8, 1.3, 0.7 Hz, H4-Ind). $^{13}C\{^1H\}$ NMR (125.7 MHz, DMSO-d_6): δ 164.3 (C=O), 144.8 (C2-Ind), 135.7 (C7a-Ind), 132.4 (C2-Ar), 131.0 (C3-Ar), 130.4 (C1-Ar), 125.9 (C3a-Ind), 122.8 (C6-Ind), 122.5 (C4-Ar), 121.8 (C5-Ind), 121.2 (C4-Ind), 111.0

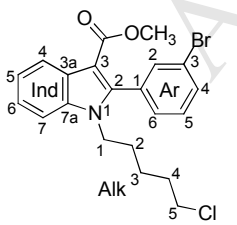
(C7-Ind), 104.4 (C3-Ind), 50.4 (OCH_3), 44.9 (C5-Alk), 43.2 (C1-Alk), 31.3 (C4-Alk), 28.3 (C2-Alk), 23.3 (C3-Alk). HRMS (MALDI) calcd. for $C_{21}H_{21}ClBrNO_2$ $[M+Cs]^+$ 567.9472, found 567.9493.

Methyl 1-(5-chloropentyl)-2-(4-fluorophenyl)-1H-indole-3-carboxylate 11d.



Reddish-brown oil; yield 1.40 g, 75%; R_f (hexane/EtOAc 2:1) 0.56; [Found: C, 67.3; H, 5.9; N, 3.7. $C_{21}H_{21}ClFNO_2$ requires C, 67.47; H, 5.66; Cl, 9.48; F, 5.08; N, 3.75]. ν_{max} (thin film) 3447, 2258, 2130, 1654, 1045, 1026, 997, 828, 767, 651 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.15-1.21 (2H, m, CH_2-Alk3), 1.48-1.58 (4H, m, CH_2-Alk2, CH_2-Alk4), 2.50 (2H, t, *J* 6.6 Hz, CH_2-Alk5), 3.62 (3H, s, OCH_3), 4.01 (2H, t, *J* 7.5 Hz, CH_2-Alk1), 7.26 (1H, ddd, *J* 7.2, 7.6, 1.0 Hz, H5-Ind), 7.30 (1H, ddd, *J* 7.6, 8.1, 1.2 Hz, H6-Ind), 7.35 (2H, dd, J_{HH} 8.8 Hz, J_{HF} 8.8 Hz, H2,H6-Ar), 7.51 (2H, dd, J_{HH} 8.8 Hz, J_{HF} 3.3 Hz, H3,H5-Ar), 7.64 (1H, br d, *J* 8.1 Hz, H7-Ind), 8.09 (1H, ddd, *J* 7.2, 1.2, 0.7 Hz, H4-Ind). $^{13}C\{^1H\}$ NMR (125.7 MHz, DMSO-d_6): δ 164.3 (C=O), 162.3 (d, $^1J_{CF}$ = 246.1 Hz, C4-Ar), 145.0 (C2-Ind), 135.6 (C7a-Ind), 132.5 (d, $^3J_{CF}$ = 8.6 Hz, C2-Ar), 127.5 (d, $^4J_{CF}$ = 3.2 Hz, C1-Ar), 125.9 (C3a-Ind), 122.7 (C6-Ind), 121.8 (C5-Ind), 121.2 (C4-Ind), 115.0 (d, $^2J_{CF}$ = 21.7 Hz, C3-Ar), 111.0 (C7-Ind), 104.4 (C3-Ind), 50.4 (OCH_3), 44.9 (C5-Alk), 43.1 (C1-Alk), 31.2 (C4-Alk), 28.3 (C2-Alk), 23.3 (C3-Alk). $^{19}F\{^1H\}$ NMR (470.5 MHz, DMSO-d_6): δ 112.6 (F). HRMS (MALDI) calcd. for $C_{21}H_{21}ClFNO_2$ $[M+Cs]^+$ 506.0294, found 506.0267.

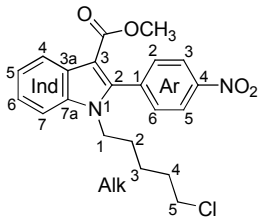
Methyl 1-(5-chloropentyl)-2-(3-bromophenyl)-1H-indole-3-carboxylate 11f.



Yellow oil; yield 1.43 g, 66%; R_f (hexane/EtOAc 2:1) 0.51; [Found: C, 57.9; H, 5.0; N, 3.0. $C_{21}H_{21}BrClNO_2$ requires C, 58.02; H, 4.87; Br, 18.38; Cl, 5.15; N, 3.22]. ν_{max} (thin film) 3440, 2256, 2130, 1654, 1044, 1028, 997, 964, 888, 780, 745, 716, 700, 655, 545 cm^{-1}. ^1H NMR (500 MHz,

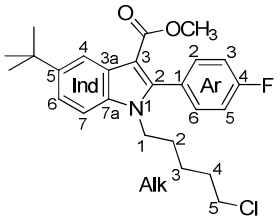
$CDCl_3$): δ_H 1.15-1.21 (2H, m, CH_2-Alk3), 1.48-1.54 (2H, m, CH_2-Alk4), 1.54-1.60 (2H, m, CH_2-Alk2), 3.47 (2H, t, *J* 6.6 Hz, CH_2-Alk5), 3.64 (3H, s, OCH_3), 4.01 (2H, t, *J* 7.5 Hz, CH_2-Alk1), 7.26 (1H, ddd, *J* 8.0, 7.9, 1.1 Hz, H5-Ind), 7.31 (1H, ddd, *J* 8.0, 8.1, 1.4 Hz, H6-Ind), 7.46-7.50 (2H, m, H5,H6-Ar), 7.64 (1H, br d, *J* 8.1 Hz, H7-Ind), 7.68-7.69 (1H, m, H2-Ar), 7.71-7.74 (1H, ddd, *J* 6.9, 2.2, 2.1 Hz, H4-Ar), 8.08 (1H, ddd, *J* 7.9, 1.4, 1.2 Hz, H4-Ind). $^{13}C\{^1H\}$ NMR (125.7 MHz, DMSO-d_6): δ 164.2 (C=O), 144.3 (C2-Ind), 135.7 (C7a-Ind), 133.5 (C1-Ar), 132.8 (C2-Ar), 131.8 (C4-Ar), 130.0 (C5-Ar), 129.4 (C6-Ar), 125.8 (C3a-Ind), 122.9 (C6-Ind), 121.9 (C5-Ind), 121.3 (C4-Ind), 121.1 (C3-Ar), 111.0 (C7-Ind), 104.5 (C3-Ind), 50.5 (OCH_3), 44.9 (C5-Alk), 43.2 (C1-Alk), 31.2 (C4-Alk), 28.3 (C2-Alk), 23.3 (C3-Alk). HRMS (MALDI) calcd. for $C_{21}H_{21}ClBrNO_2$ $[M+Na]^+$ 456.0336;458.0316, found 456.0348;458.0332.

Methyl 1-(5-chloropentyl)-2-(4-nitrophenyl)-1H-indole-3-carboxylate 11g.



Yellow oil; yield 1.80 g, 90%; R_f (hexane/EtOAc 2:1) 0.48; [Found: C, 62.8; H, 5.5; N, 7.2. $C_{21}H_{21}ClN_2O_4$ requires C, 62.92; H, 5.28; Cl, 8.84; N, 6.99]. ν_{max} (thin film) 3500, 2861, 1696, 1602, 1047, 1021, 995, 858, 758, 702 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$): δ_H 1.15-1.20 (2H, m, CH_2-Alk3), 1.47-1.52 (2H, m, CH_2-Alk4), 1.53-1.58 (2H, m, CH_2-Alk2), 3.46 (2H, t, *J* 6.6 Hz, CH_2-Alk5), 3.63 (3H, s, OCH_3), 4.05 (2H, t, *J* 7.4 Hz, CH_2-Alk1), 7.29 (1H, dd, *J* 7.1, 7.9 Hz, H5-Ind), 7.34 (1H, ddd, *J* 7.1, 8.2, 1.3 Hz, H6-Ind), 7.69 (1H, br d, *J* 8.2 Hz, H7-Ind), 7.79 (2H, d, *J* 8.7 Hz, H2,H6-Ar), 8.10 (1H, br d, *J* 7.9 Hz, H4-Ind), 8.37 (2H, d, *J* 8.7 Hz, H3,H5-Ar). $^{13}C\{^1H\}$ NMR (150.9 MHz, DMSO-d_6): δ 164.2 (C=O), 147.7 (C4-Ar), 143.6 (C2-Ind), 138.1 (C1-Ar), 136.0 (C7a-Ind), 132.0 (C2-Ar), 125.8 (C3a-Ind), 123.2 (C6-Ind), 123.0 (C3-Ar), 122.1 (C5-Ind), 121.3 (C4-Ind), 111.2 (C7-Ind), 104.9 (C3-Ind), 50.6 (OCH_3), 44.9 (C5-Alk), 43.3 (C1-Alk), 31.2 (C4-Alk), 28.3 (C2-Alk), 23.2 (C3-Alk).

Methyl 5-tert-butyl-1-(5-chloropentyl)-2-(4-fluorophenyl)-1H-indole-3-carboxylate 11i.



Yellow oil; yield 1.68 g, 78%; R_f (hexane/EtOAc 2:1) 0.58; [Found: C, 69.6; H, 7.0; N, 3.1. $C_{25}H_{29}ClFNO_2$ requires C, 69.84; H, 6.80; Cl, 8.25; F, 4.42; N, 3.26]. ν_{max} (thin film) 3593, 3182, 2260, 2131, 1644, 1046, 1024, 983, 830, 772, 742, 721, 669, 649 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ_H 1.15-1.21 (2H, m, CH_2-Alk3), 1.37 (9H, s, $(CH_3)_3$), 1.48-1.57 (4H, m, CH_2-Alk2, CH_2-Alk4), 3.48 (2H, t, *J* 6.6 Hz, CH_2-Alk5), 3.59 (3H, s, OCH_3), 3.97 (2H, t, *J* 7.5 Hz, CH_2-Alk1), 7.34 (2H, dd, J_{HH} 8.9 Hz, J_{HF} 8.9 Hz, H2,H6-Ar), 7.38 (1H, dd, *J* 8.7, 2.0 Hz, H6-Ind), 7.47 (2H, dd, J_{HH} 8.9 Hz, J_{HF} 3.3 Hz, H3,H5-Ar), 7.53 (1H, dd, *J* 8.7, 0.4 Hz, H7-Ind), 8.11 (1H, dd, *J* 2.0, 0.4 Hz, H4-Ind). $^{13}C\{^1H\}$ NMR (125.7 MHz, DMSO-d_6): δ 164.5 (C=O), 162.3 (d, $^1J_{CF}$ = 245.8 Hz, C4-Ar), 144.9 (C2-Ind), 144.3 (C5-Ind), 133.9 (C7a-Ind), 132.5 (d, $^3J_{CF}$ = 8.4 Hz, C2-Ar), 127.7 (d, $^4J_{CF}$ = 3.2 Hz, C1-Ar), 125.8 (C3a-Ind), 120.8 (C6-Ind), 116.8 (C4-Ind), 115.0 (d, $^2J_{CF}$ = 21.7 Hz, C3-Ar), 110.4 (C7-Ind), 104.3 (C3-Ind), 50.3 (OCH_3), 44.9 (C5-Alk), 43.1 (C1-Alk), 34.4 ($\underline{C}(CH_3)_3$), 31.6 ($C(\underline{C}H_3)_3$), 31.2 (C4-Alk), 28.3 (C2-Alk), 23.3 (C3-Alk). $^{19}F\{^1H\}$ NMR (470.5 MHz, DMSO-d_6): δ 112.7 (F). HRMS (MALDI) calcd. for $C_{25}H_{29}ClFNO_2$ $[M+H]^+$ 430.1944, found 430.1953.

ACKNOWLEDGMENT

This work was supported by the Russian scientific foundation (grant № 14-23-00073).

SUPPLEMENTARY DATA

1D and 2D NMR spectra for all compounds. Supplementary data related to this article can be found at …

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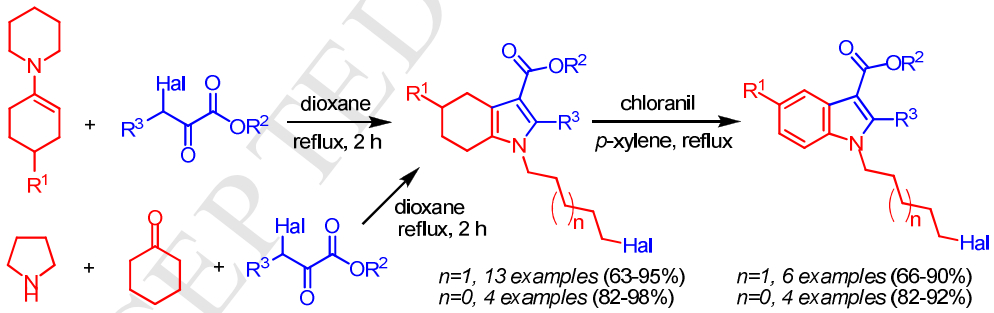
Graphical abstract

Sequential substitution/ring cleavage/addition reaction of 1-(cyclohex-1-enyl)-piperidine and -pyrrolidine with chloropyruvates for the efficient synthesis of substituted 4,5,6,7-tetrahydro-1*H*-indole derivatives

Vakhid A. Mamedov,* Elena A.Hafizova, Anastasiya I. Zamaletdinova, Il'dar Kh. Rizvanov, Alla B. Mirgorodskaya, Lucia Ya. Zakharova, Shamil K. Latypov, Oleg G. Sinyashin



SUPPORTING INFORMATION FOR:

Sequential substitution/ring cleavage/addition reaction of 1-(cyclohex-1-enyl)-piperidine and -pyrrolidine with chloropyruvates for the efficient synthesis of substituted 4,5,6,7-tetrahydro-1*H*-indole derivatives

Vakhid A. Mamedov,[a,b,*] Elena A.Hafizova,[a,b] Anastasiya I. Zamaletdinova,[a,b] Il'dar Kh. Rizvanov,[a] Alla B. Mirgorodskaya,[a,b] Lucia Ya. Zakharova,[a,b] Shamil K. Latypov,[a] Oleg G. Sinyashin[a,b]

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General Methods

All NMR experiments were performed with a 600, 500 and 400 MHz (600, 500 and 400 MHz for ^{1}H NMR; 100 MHz for ^{13}C NMR; 60 MHz for ^{15}N NMR, respectively) spectrometers equipped with a 5 mm diameter gradient inverse broad band probehead and a pulsed gradient unit capable of producing magnetic field pulse gradients in the z-direction of 53.5 G·cm^{-1}. NMR experiments were carried out at 303 K. DPFGROE and TOCSY spectra were obtained using a Hermite-shaped pulse for selective excitation. Chemical shifts (δ in ppm) are referenced to the solvents ($CDCl_3$ (δ = 7.27 ppm for ^{1}H and 77.0 ppm for ^{13}C NMR) or DMSO-d_6 (δ = 2.49 ppm for ^{1}H and 39.5 ppm for ^{13}C NMR)), to external CD_3NO_2 (380.2 ppm) for ^{15}N NMR spectra (conversion factor to NH_3: -380.2 ppm) and to external C_6F_6 (-164.9 ppm) for ^{19}F NMR spectra.

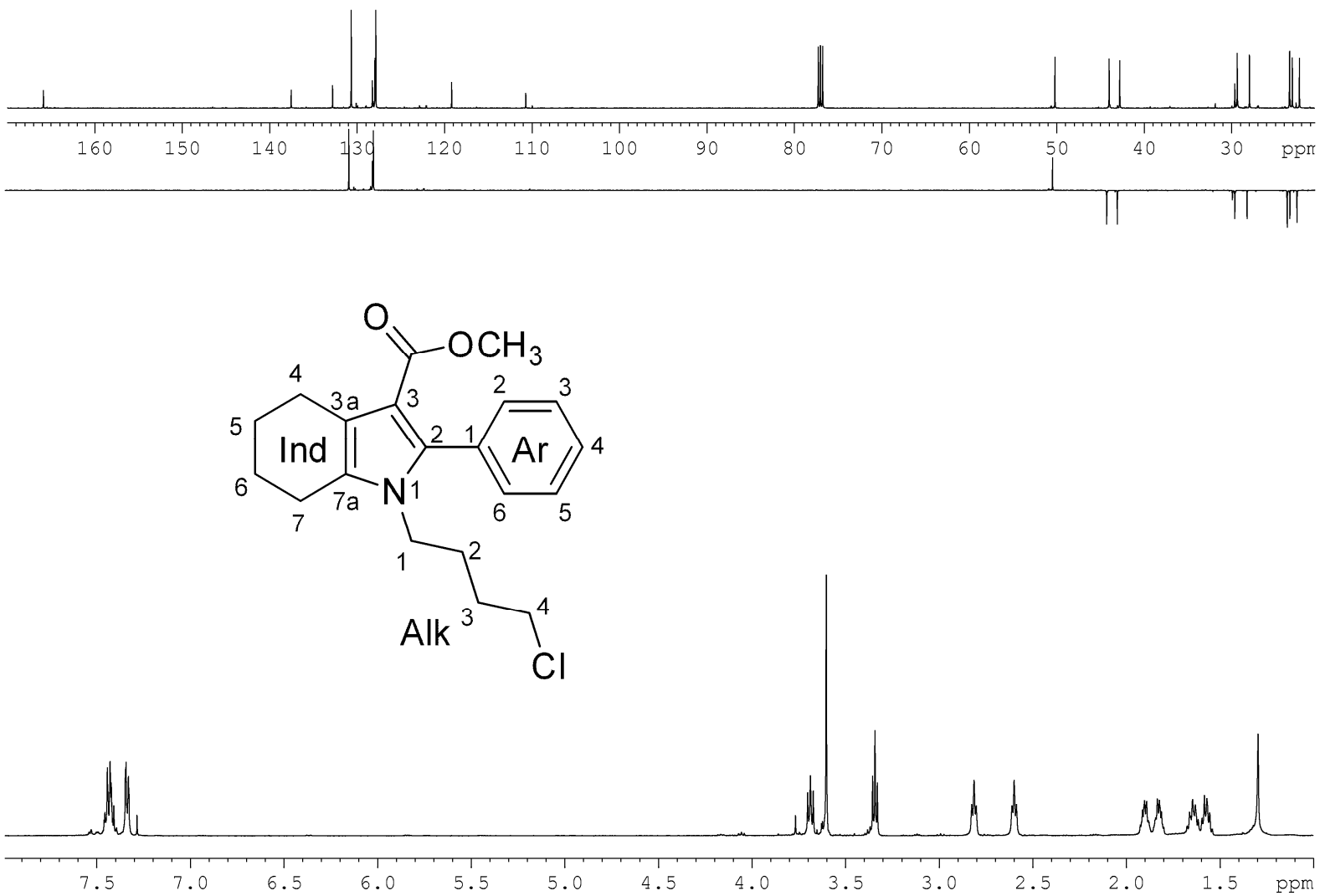

Figure S1. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **3a** in $CDCl_3$ at T = 303 K.

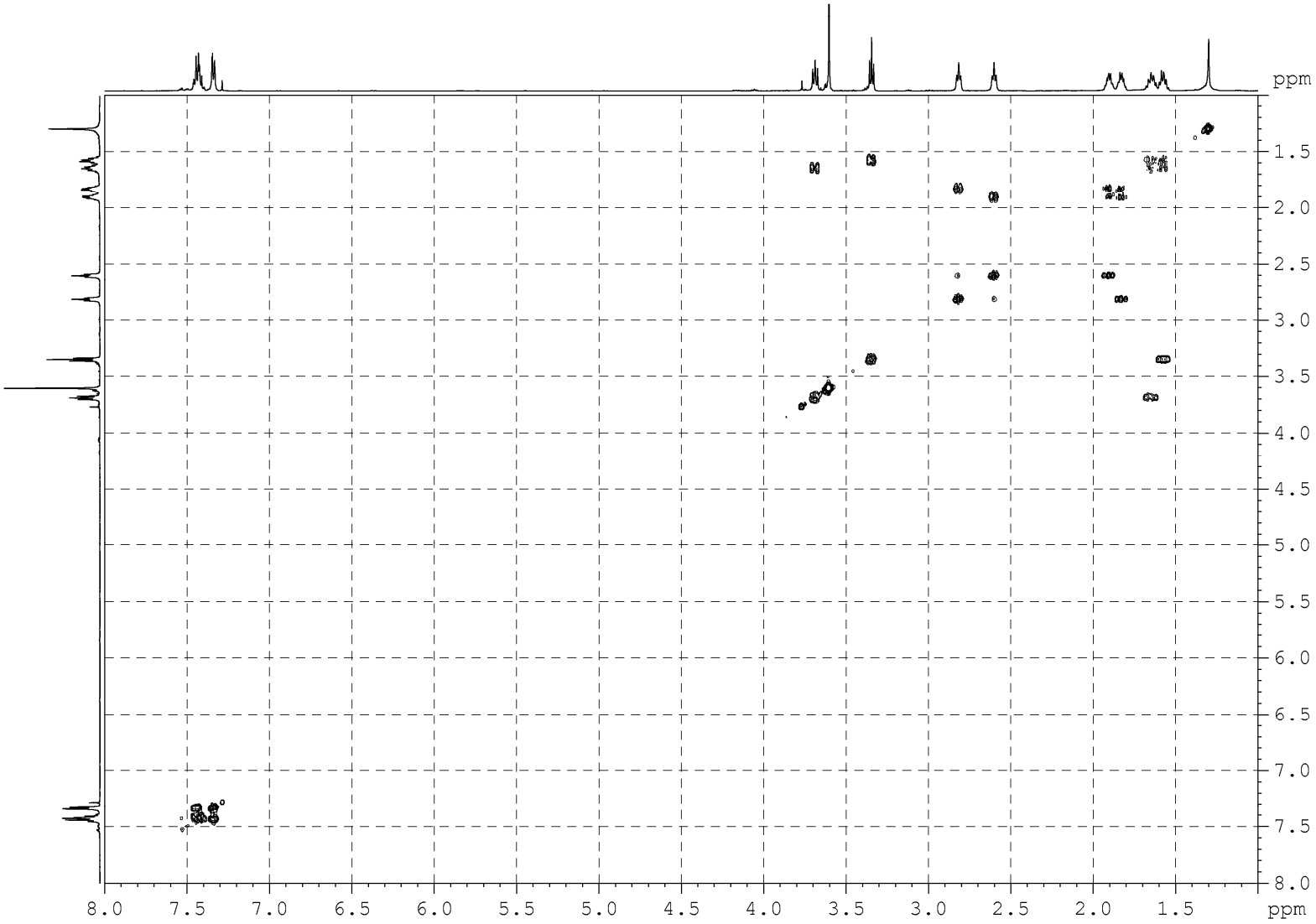

Figure S2. 2D ^{1}H-^{1}H COSY NMR spectra of **3a** in $CDCl_3$ at T = 303 K.

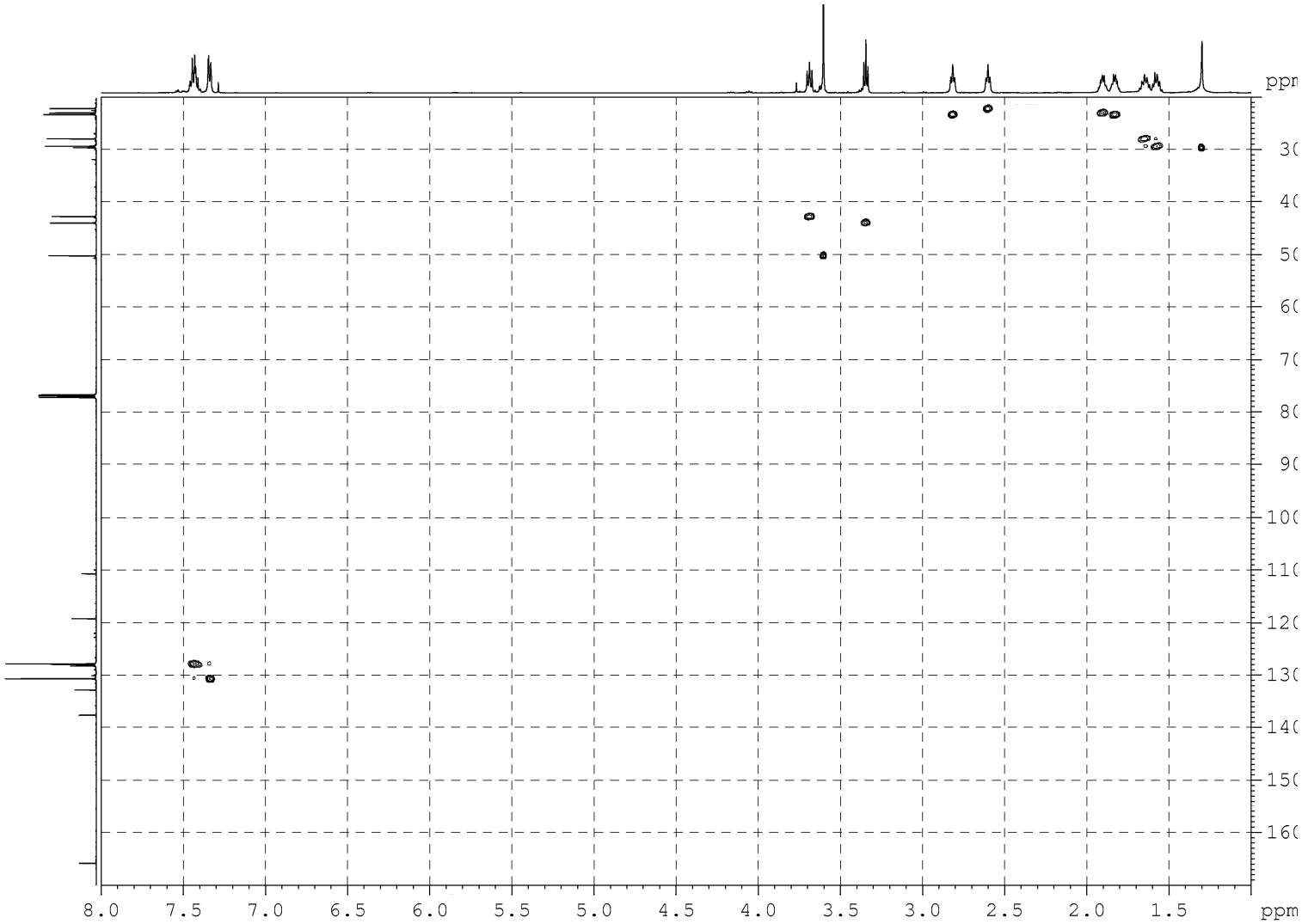

Figure S3. 2D ^{1}H-^{13}C HSQC NMR spectra of **3a** in $CDCl_3$ at T = 303 K.

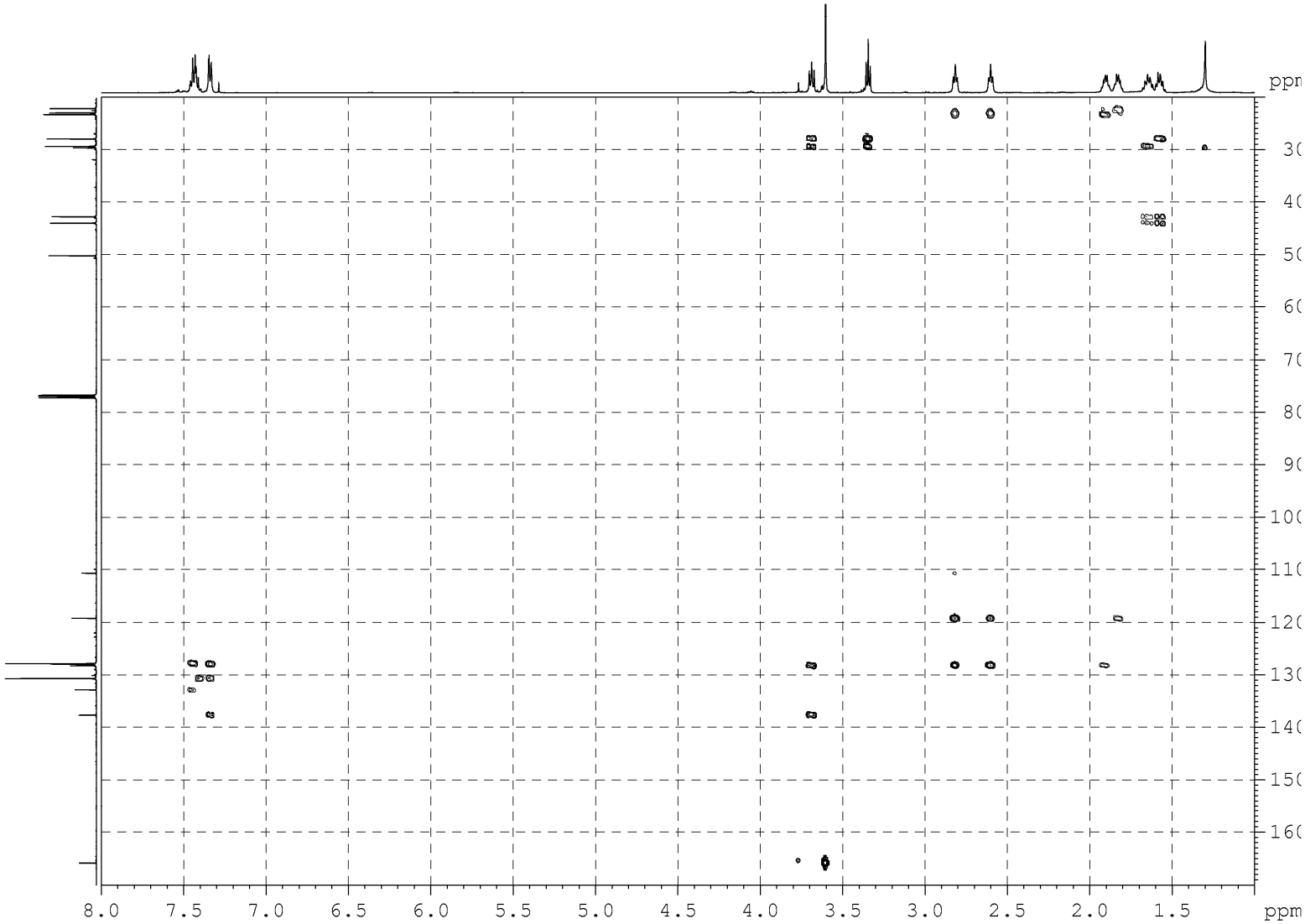

Figure S4. 2D ^{1}H-^{13}C HMBC NMR spectra of **3a** in $CDCl_3$ at T = 303 K.

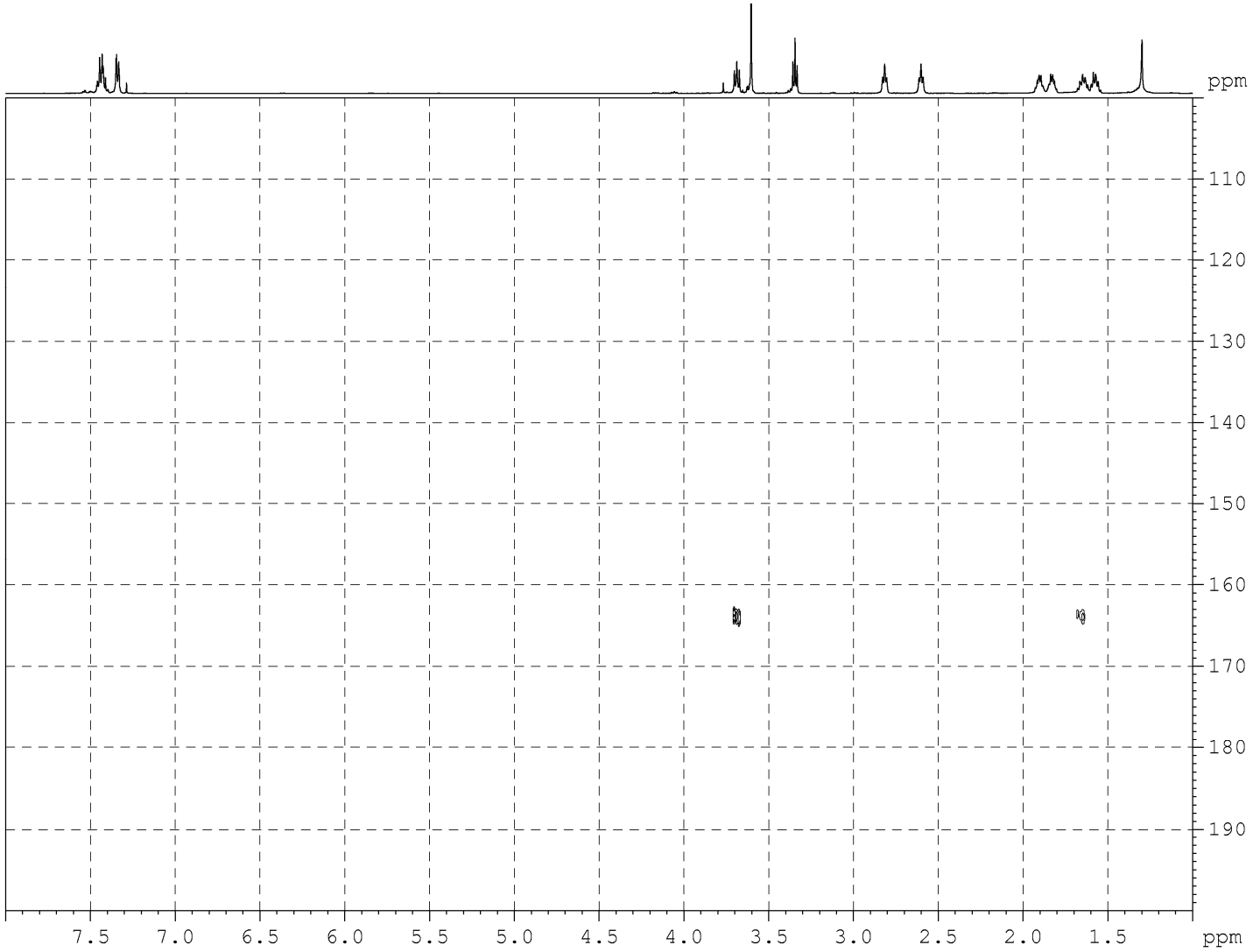

Figure S5. 2D ^{1}H-^{15}N HMBC NMR spectra of **3a** in $CDCl_3$ at T = 303 K.

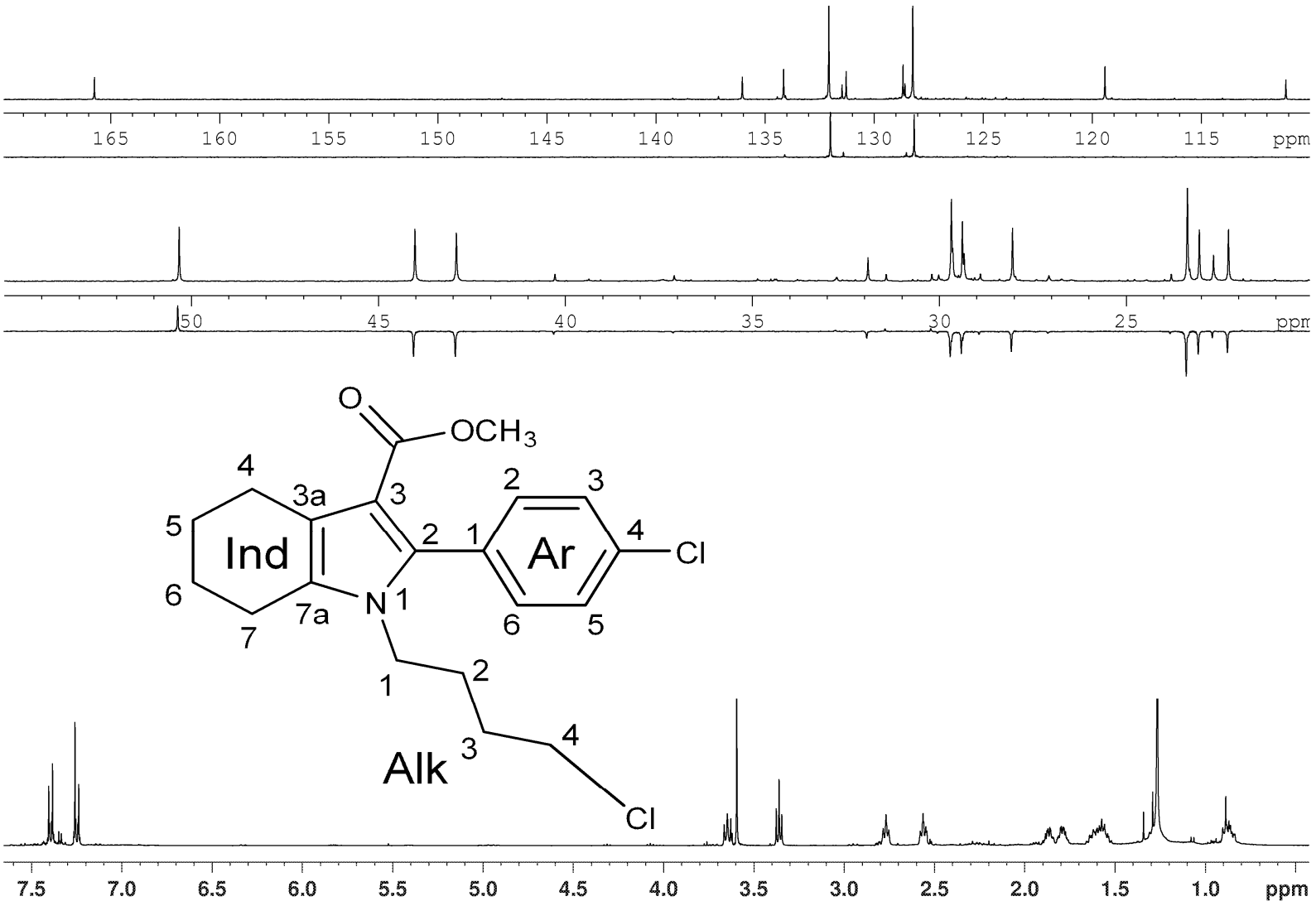

Figure S6. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **3b** in $CDCl_3$ at T = 303 K.

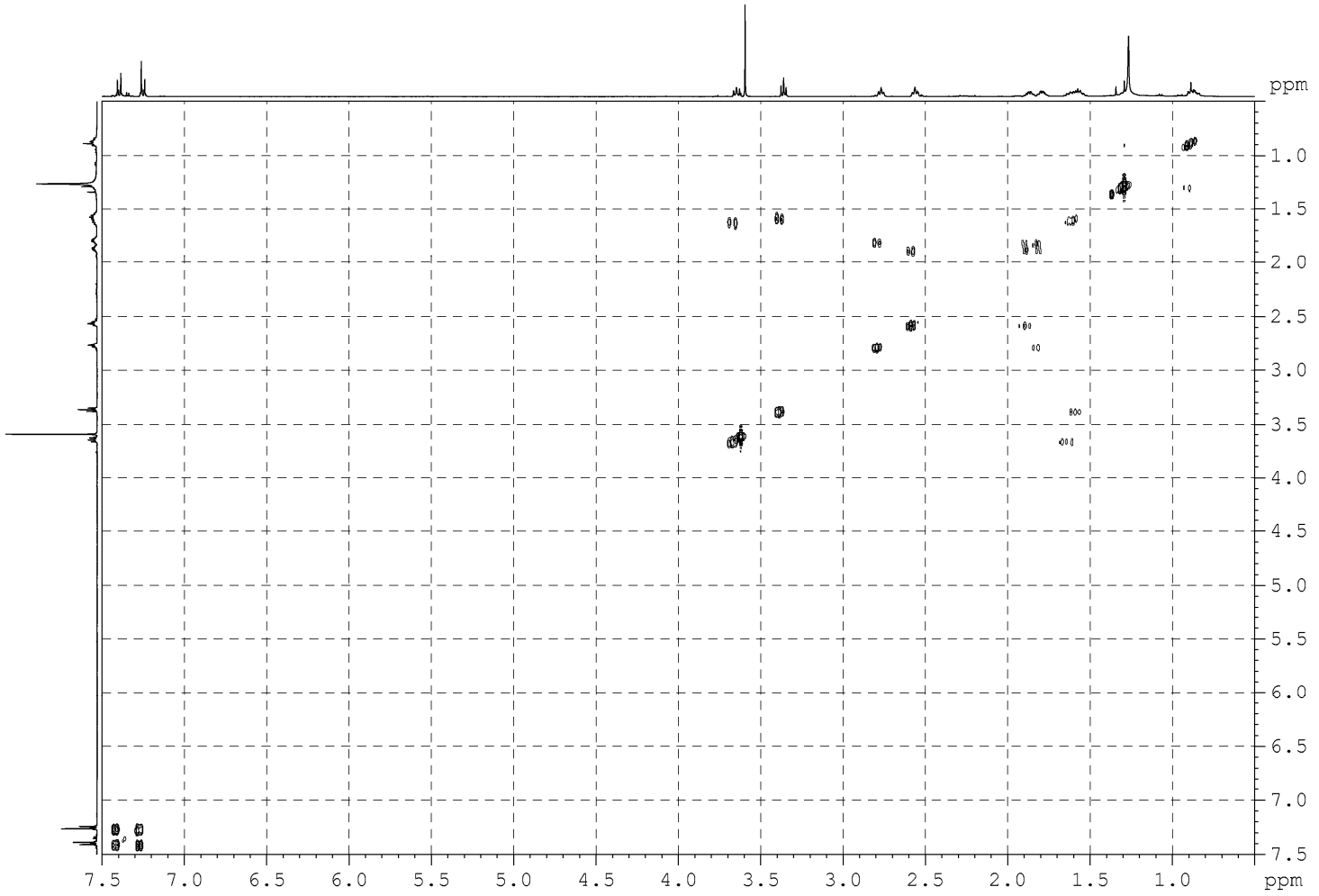

Figure S7. 2D ^{1}H-^{1}H COSY NMR spectra of **3b** in $CDCl_3$ at T = 303 K.

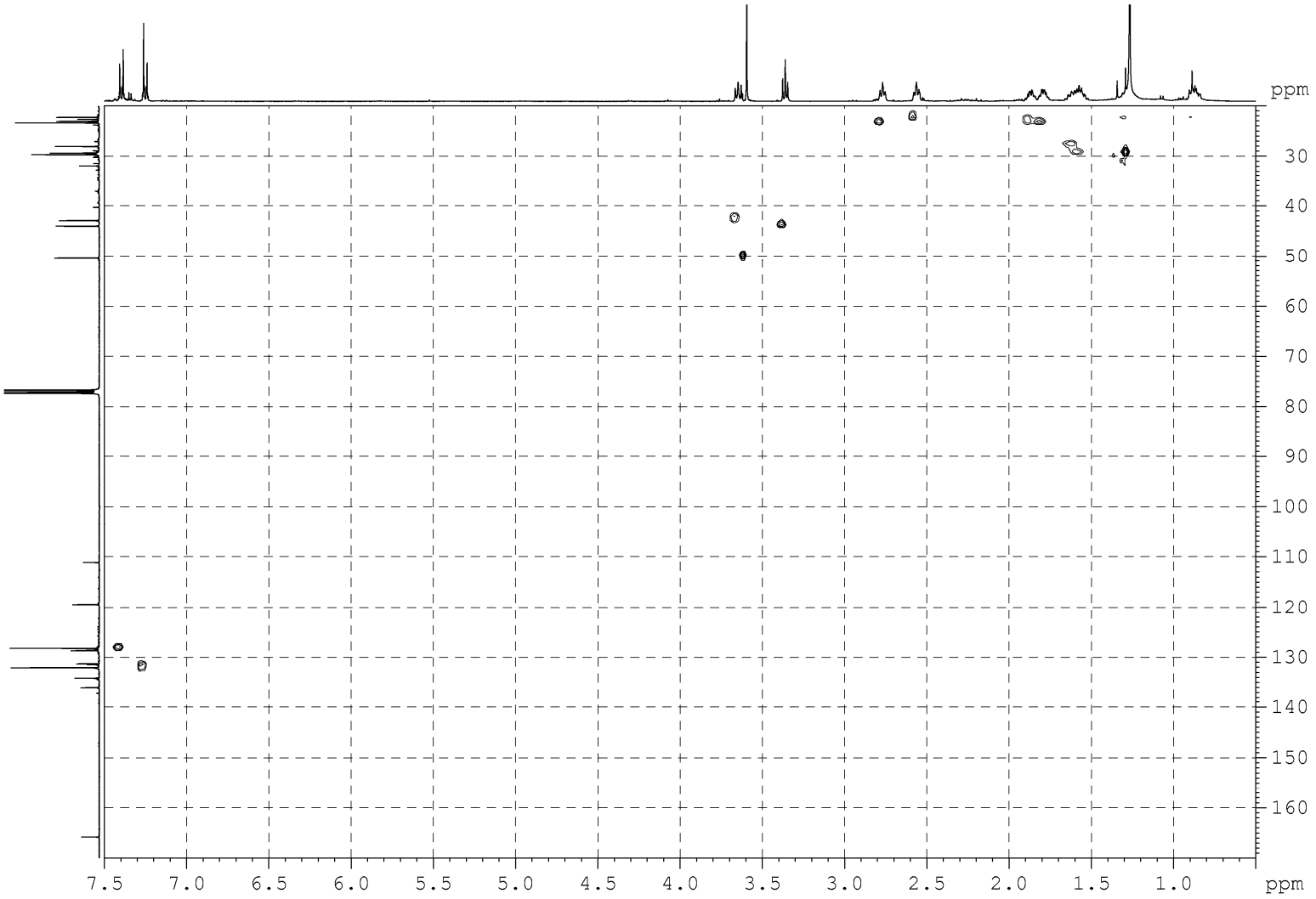

Figure S8. 2D ^{1}H-^{13}C HSQC NMR spectra of **3b** in $CDCl_3$ at T = 303 K.

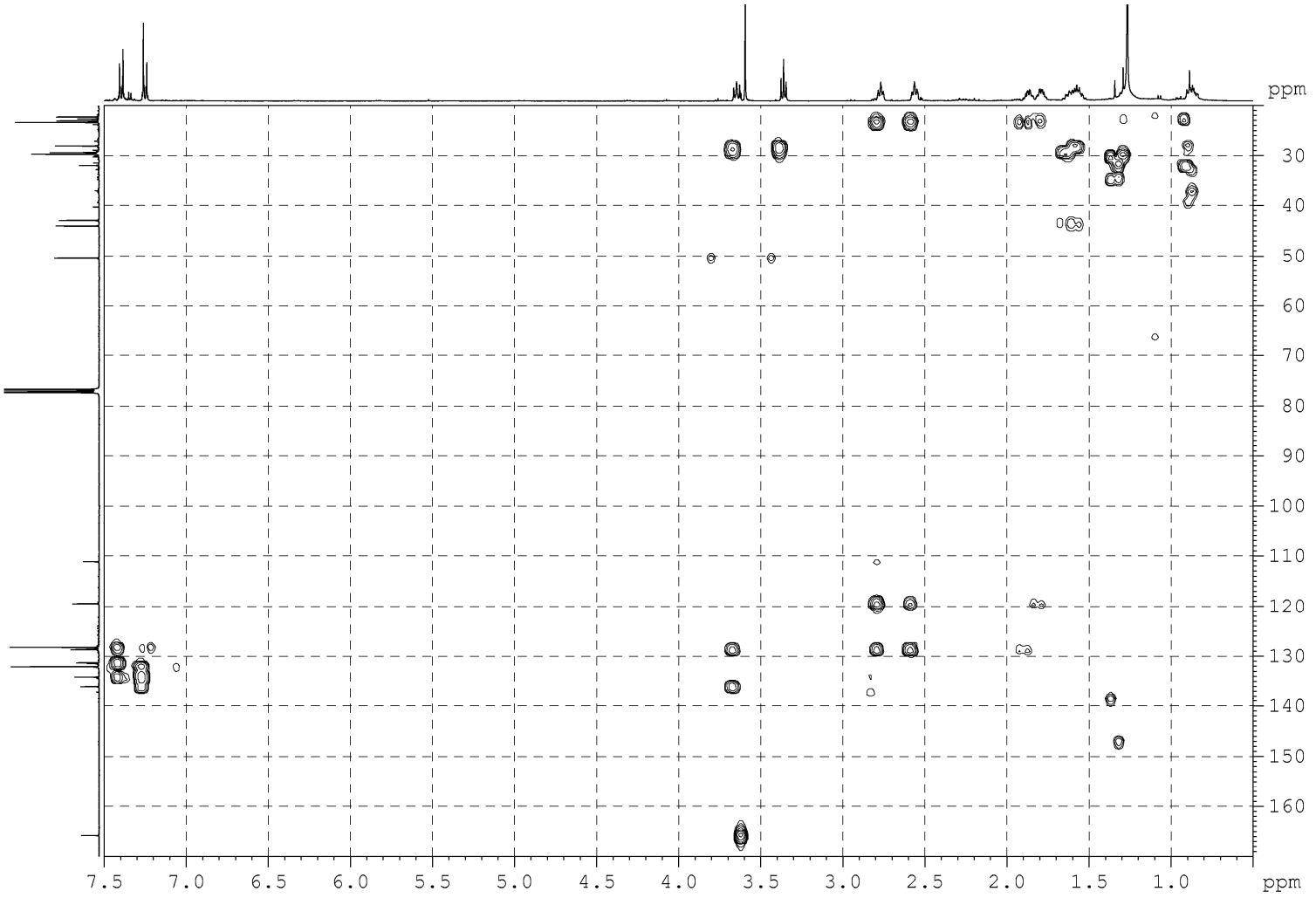

Figure S9. 2D ^{1}H-^{13}C HMBC NMR spectra of **3b** in $CDCl_3$ at T = 303 K.

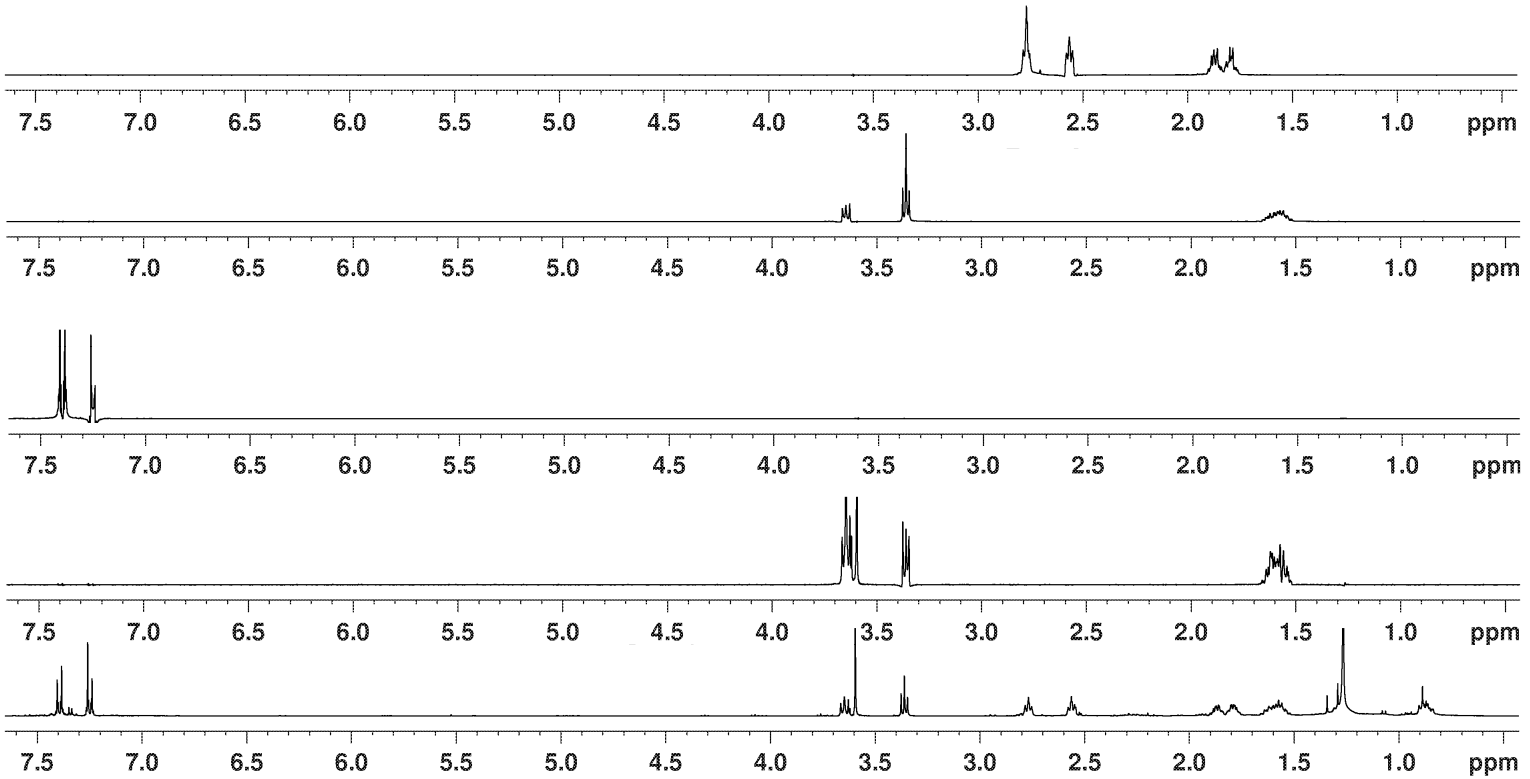

Figure S10. 1D ^{1}H and ^{1}H TOCSY NMR spectra of **3b** in $CDCl_3$ at T = 303 K.

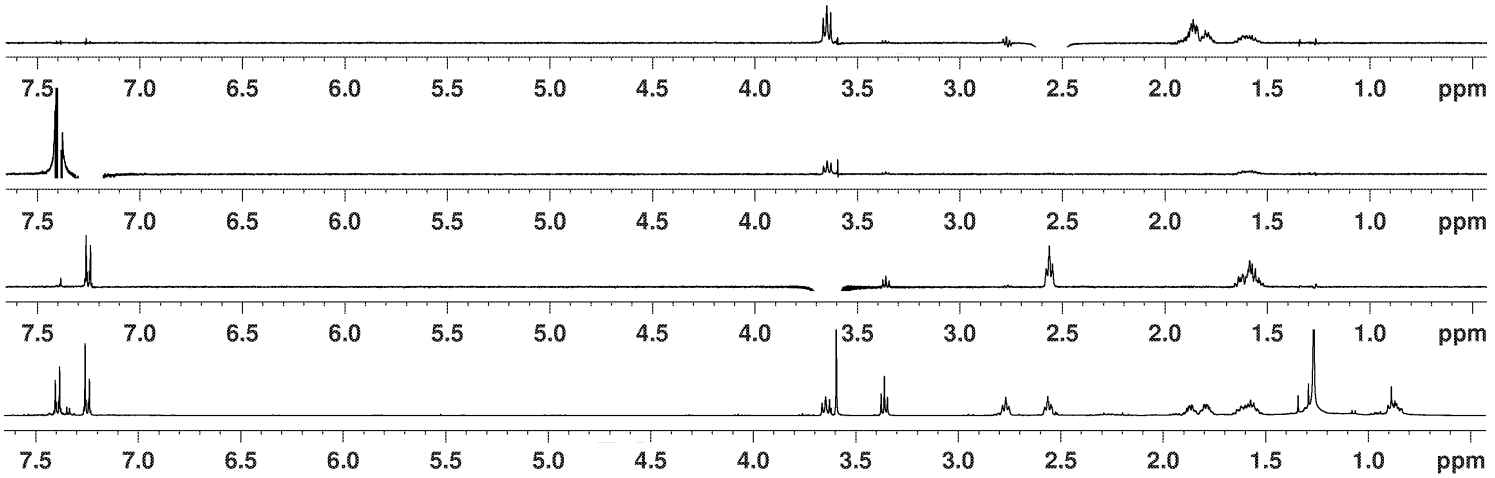

Figure S11. 1D ^{1}H and ^{1}H DPFGROE NMR spectra of **3b** in $CDCl_3$ at T = 303 K.

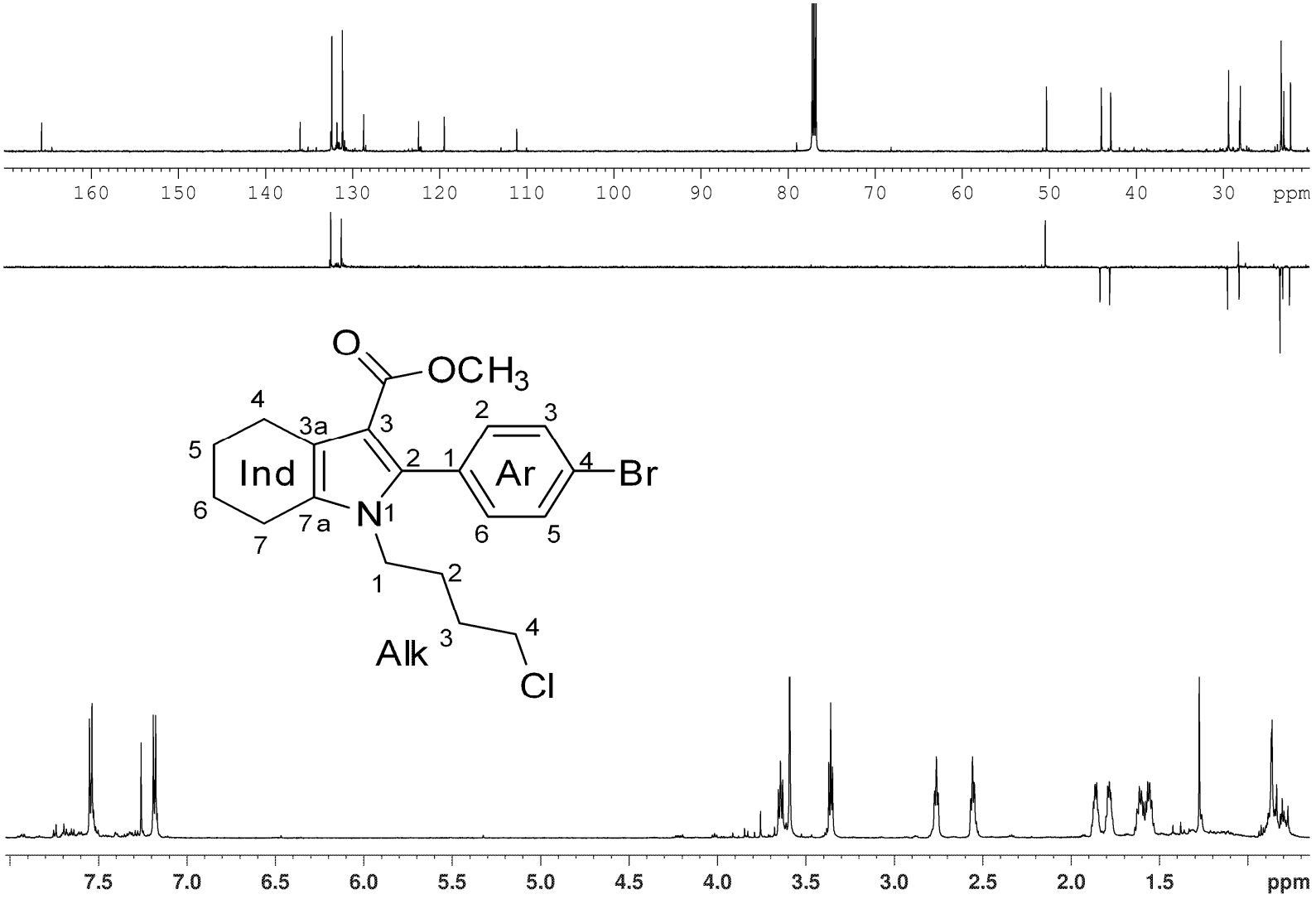

Figure S12. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **3c** in $CDCl_3$ at T = 303 K.

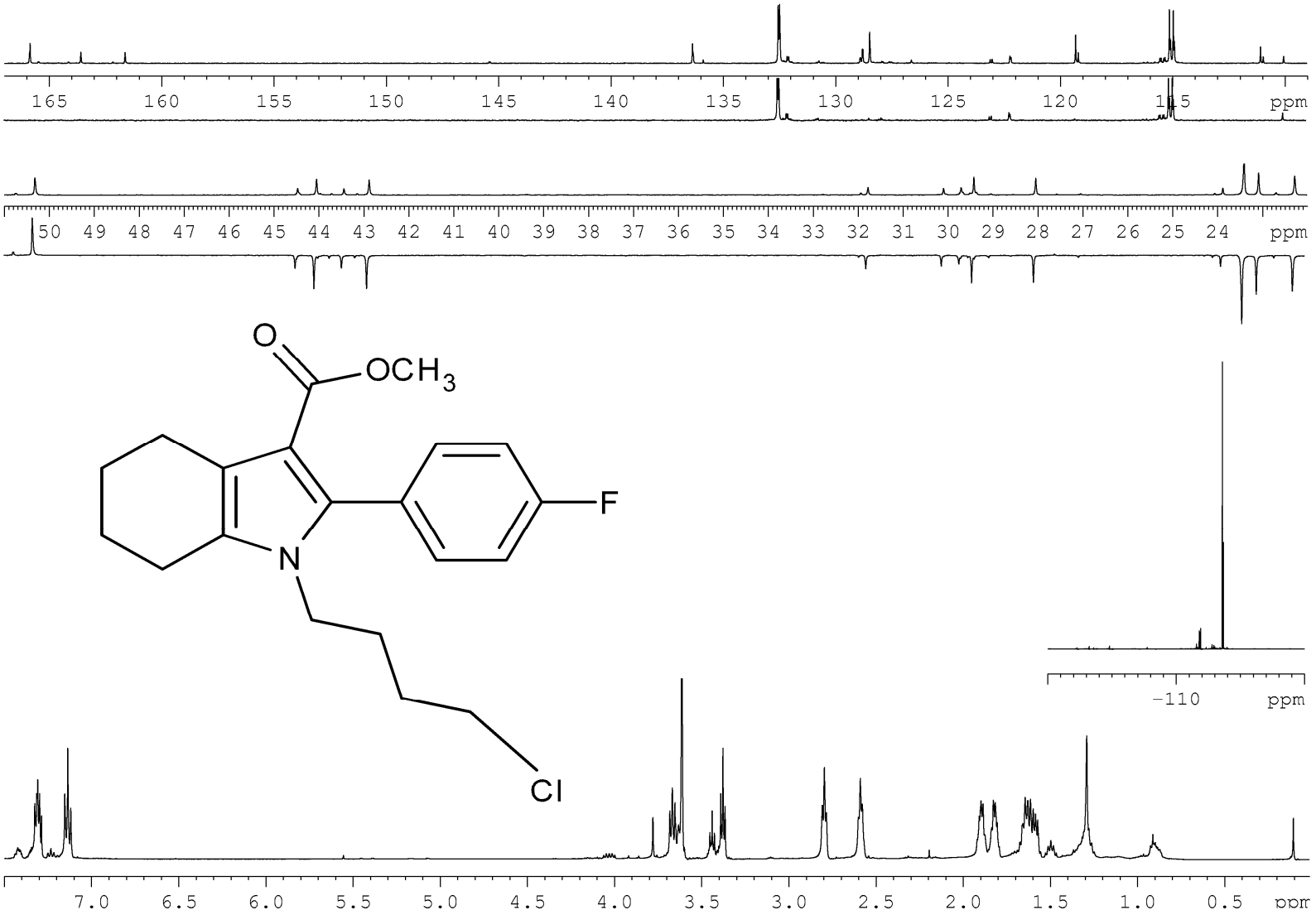

Figure S13. 1D ^{1}H, ^{13}C DEPT, $^{13}C\{^{1}H\}$ and $^{19}F\{^{1}H\}$ NMR spectra of **3d** in $CDCl_3$ at T = 303 K.

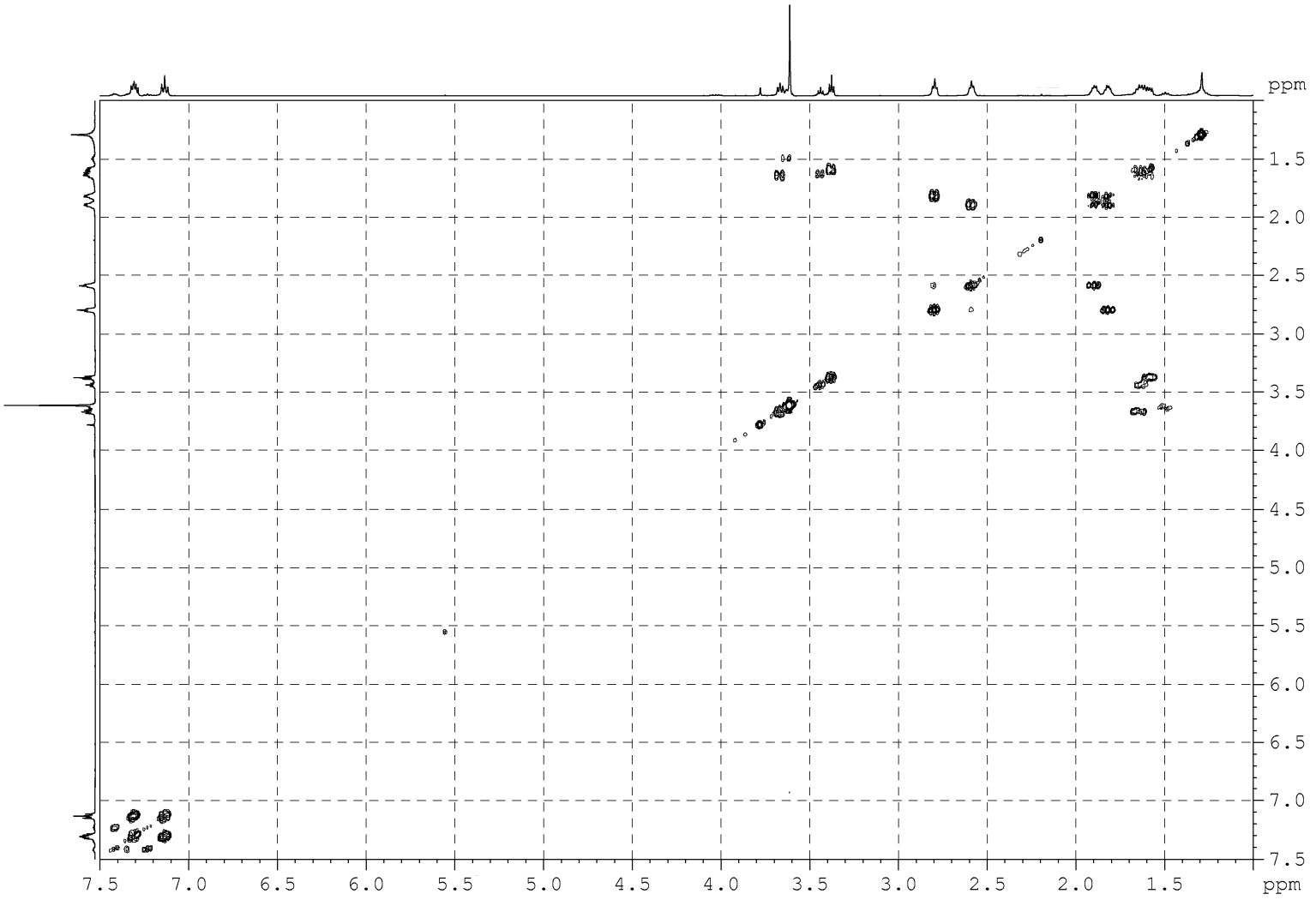

Figure S14. 2D ^{1}H-^{1}H COSY NMR spectra of **3d** in $CDCl_3$ at T = 303 K.

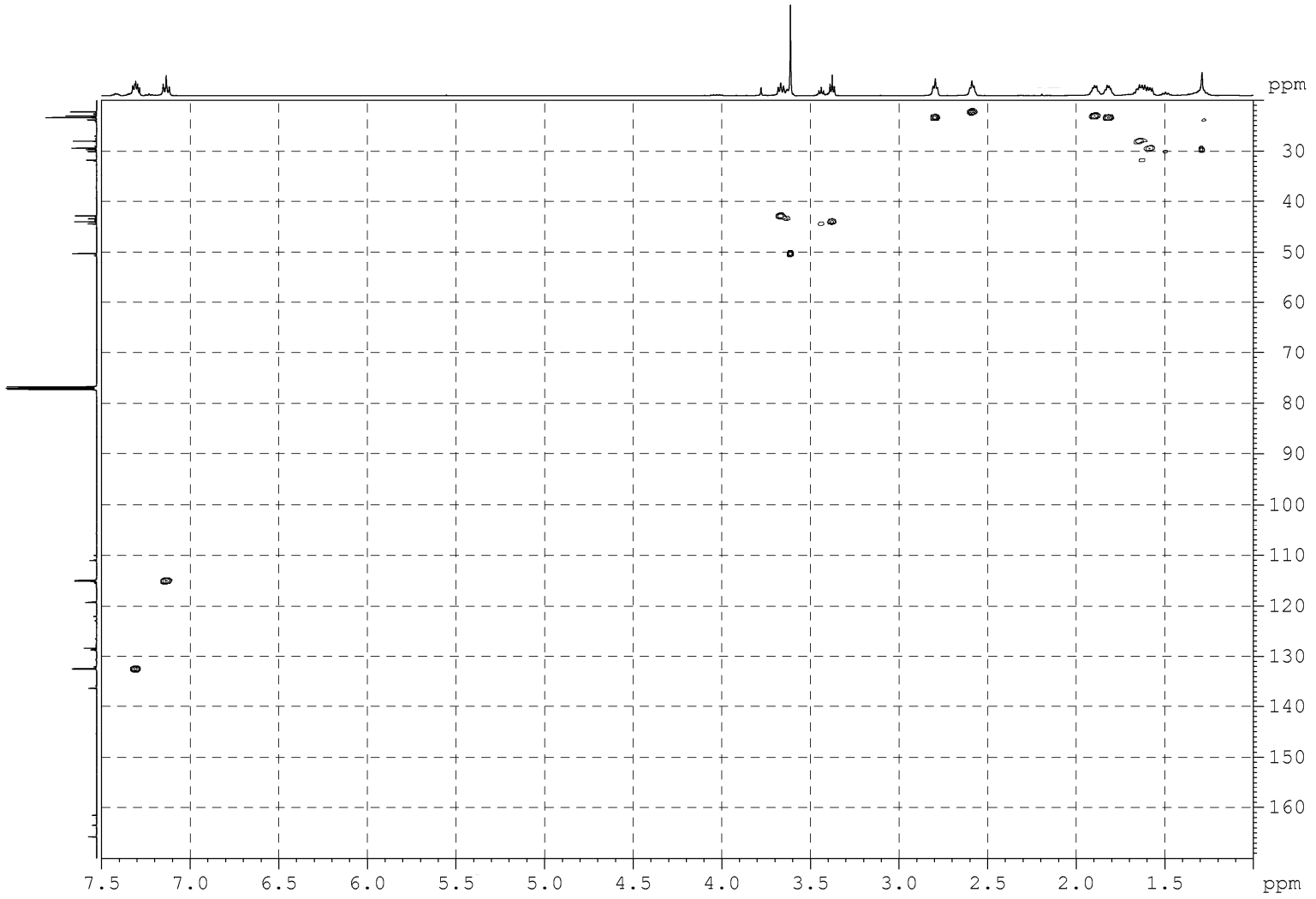

Figure S15. 2D ^{1}H-^{13}C HSQC NMR spectra of **3d** in $CDCl_3$ at T = 303 K.

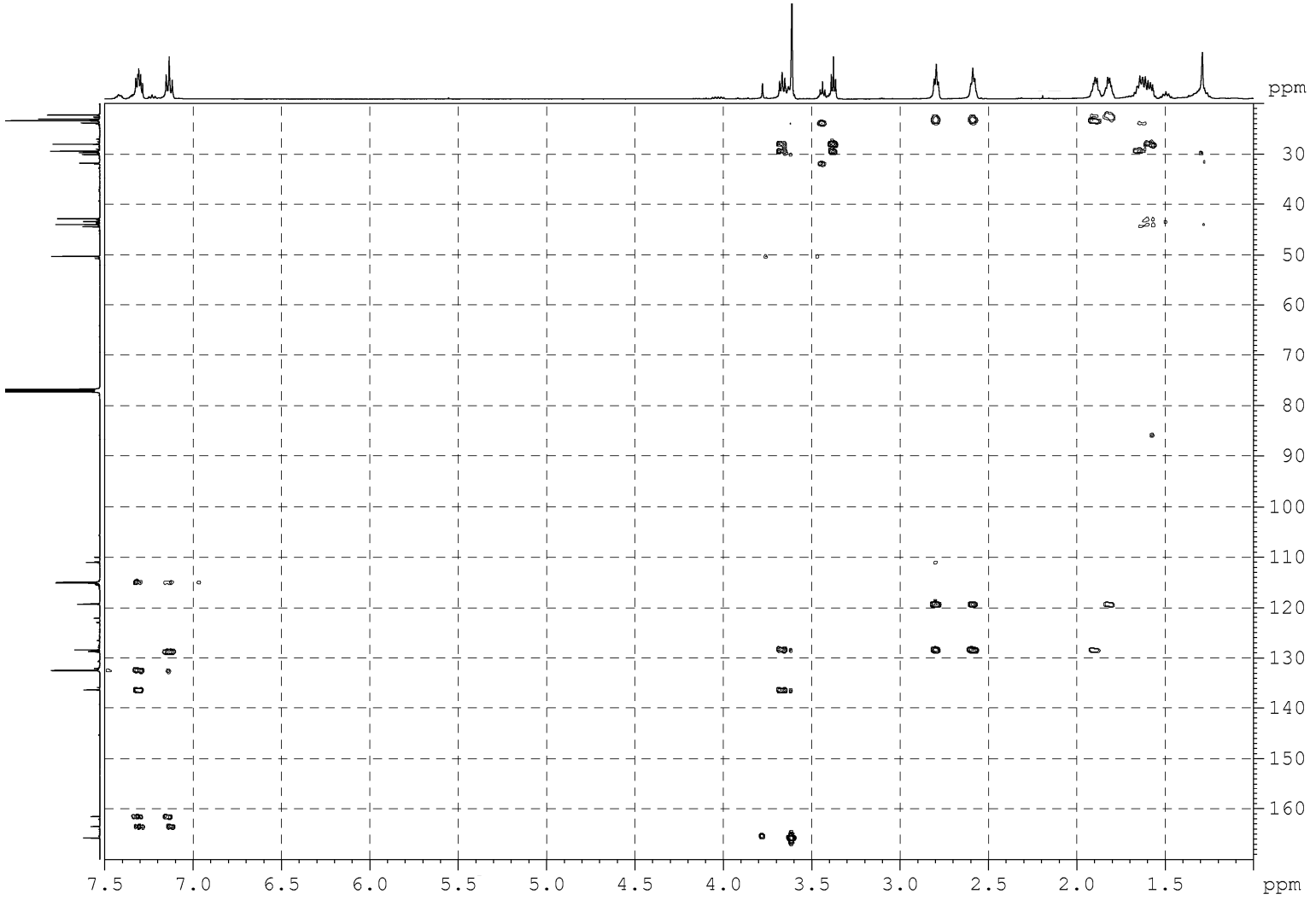

Figure S16. 2D ^{1}H-^{13}C HMBC NMR spectra of **3d** in $CDCl_3$ at T = 303 K.

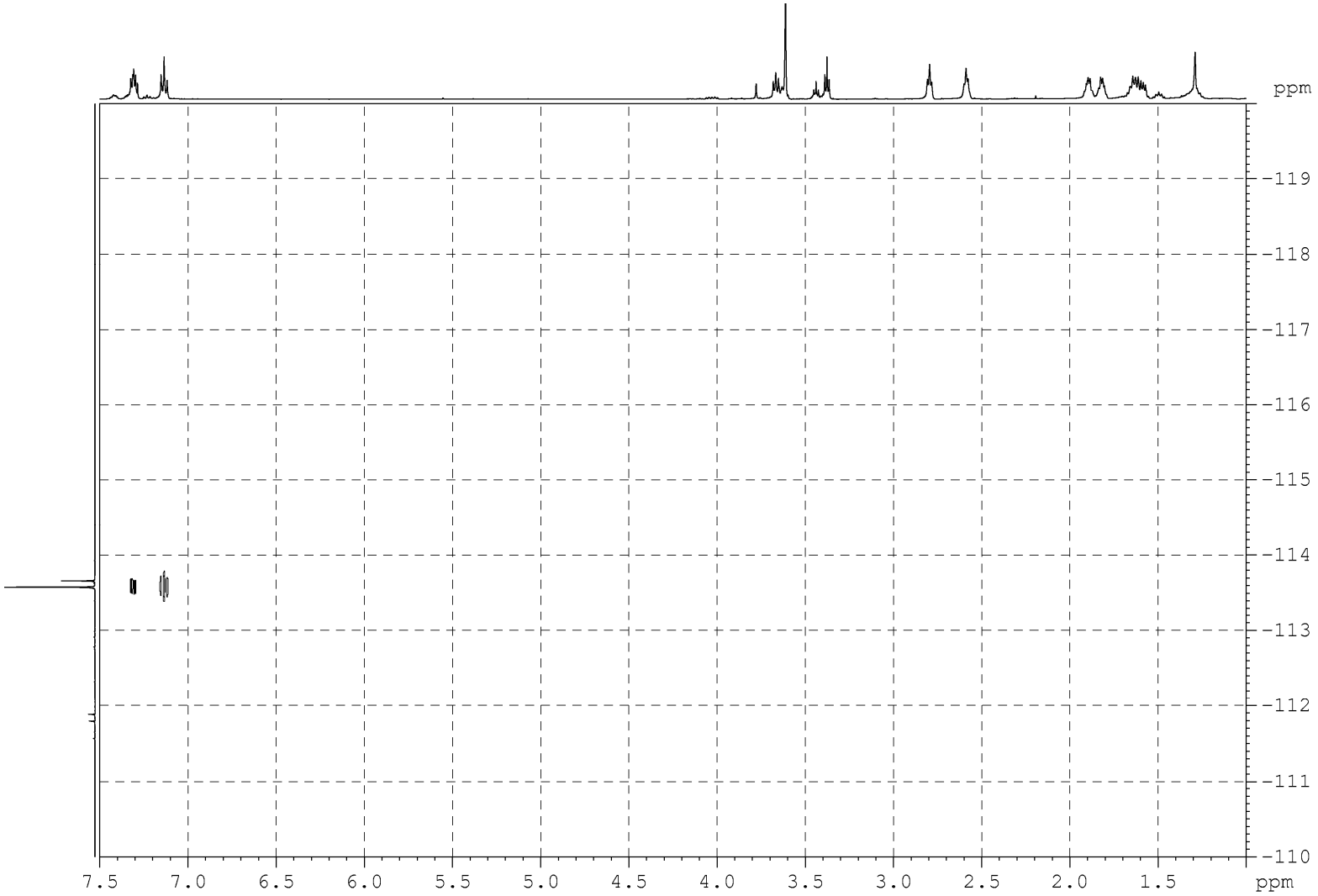

Figure S17. 2D ^{1}H-^{19}F HMBC NMR spectra of **3d** in $CDCl_3$ at T = 303 K.

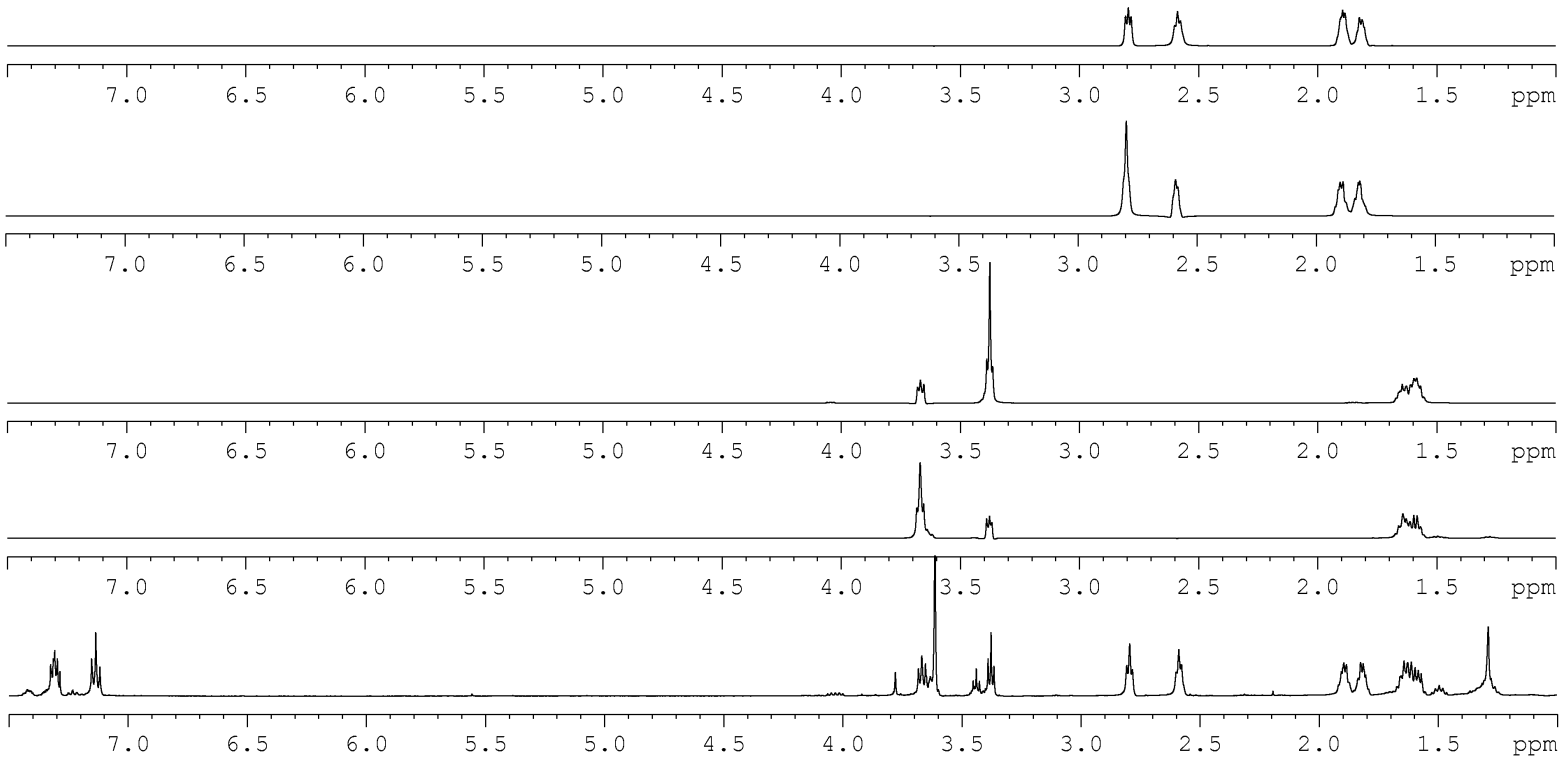

Figure S18. 1D ^{1}H and ^{1}H TOCSY NMR spectra of **3d** in $CDCl_3$ at T = 303 K.

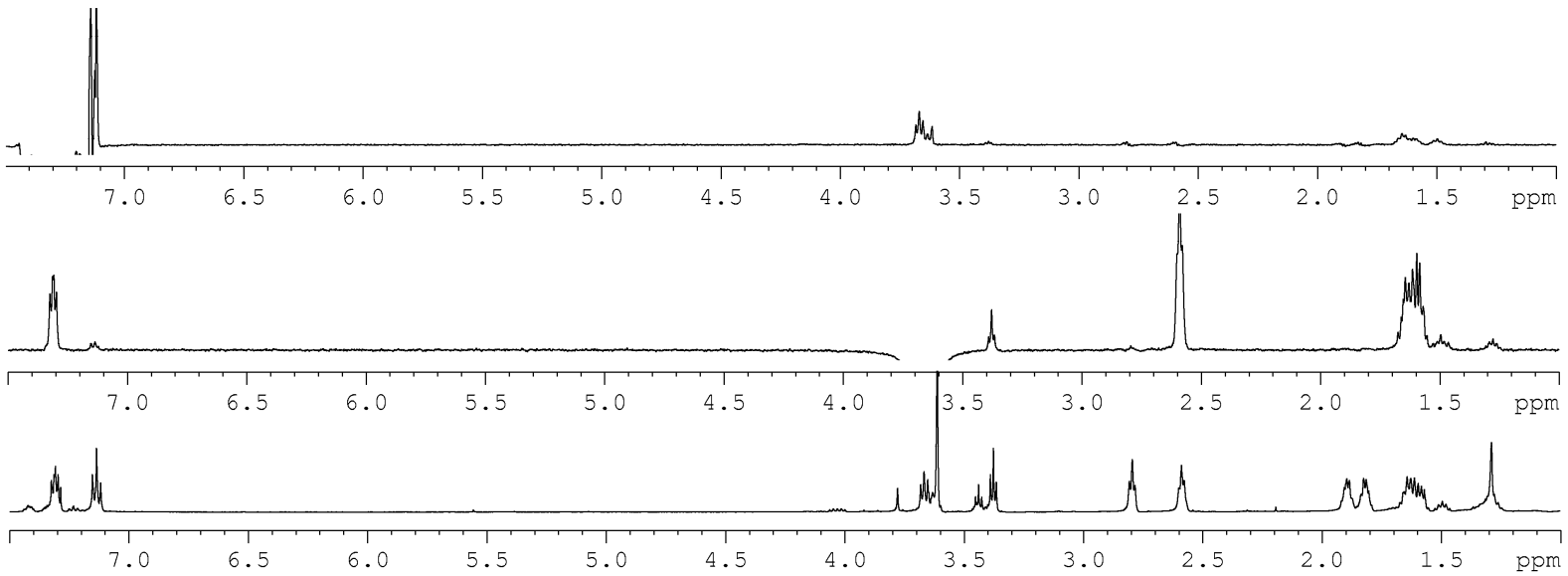

Figure S19. 1D ^{1}H and ^{1}H DPFGROE NMR spectra of **3d** in $CDCl_3$ at T = 303 K.

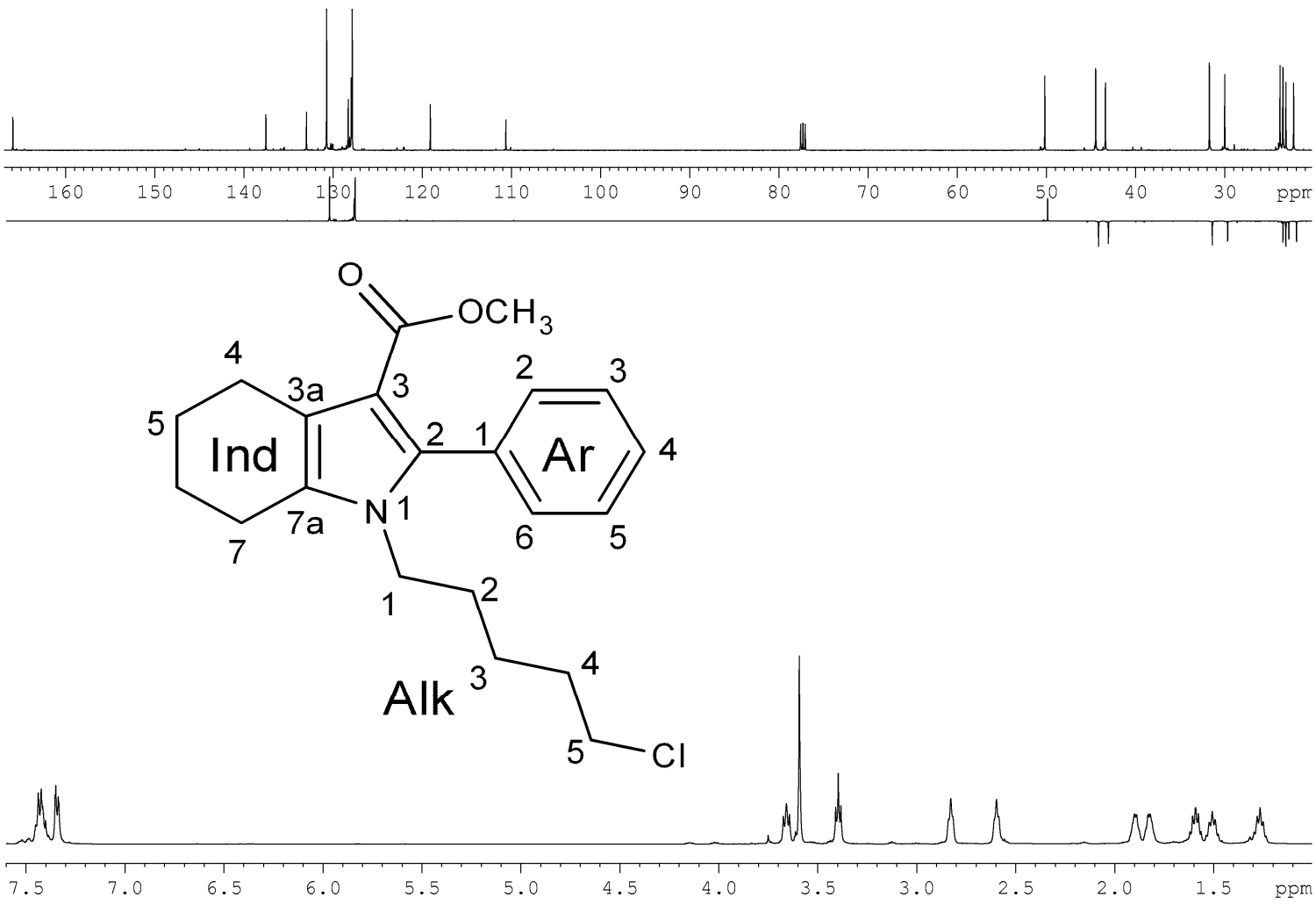

Figure S20. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **5a** in $CDCl_3$ at T = 303 K.

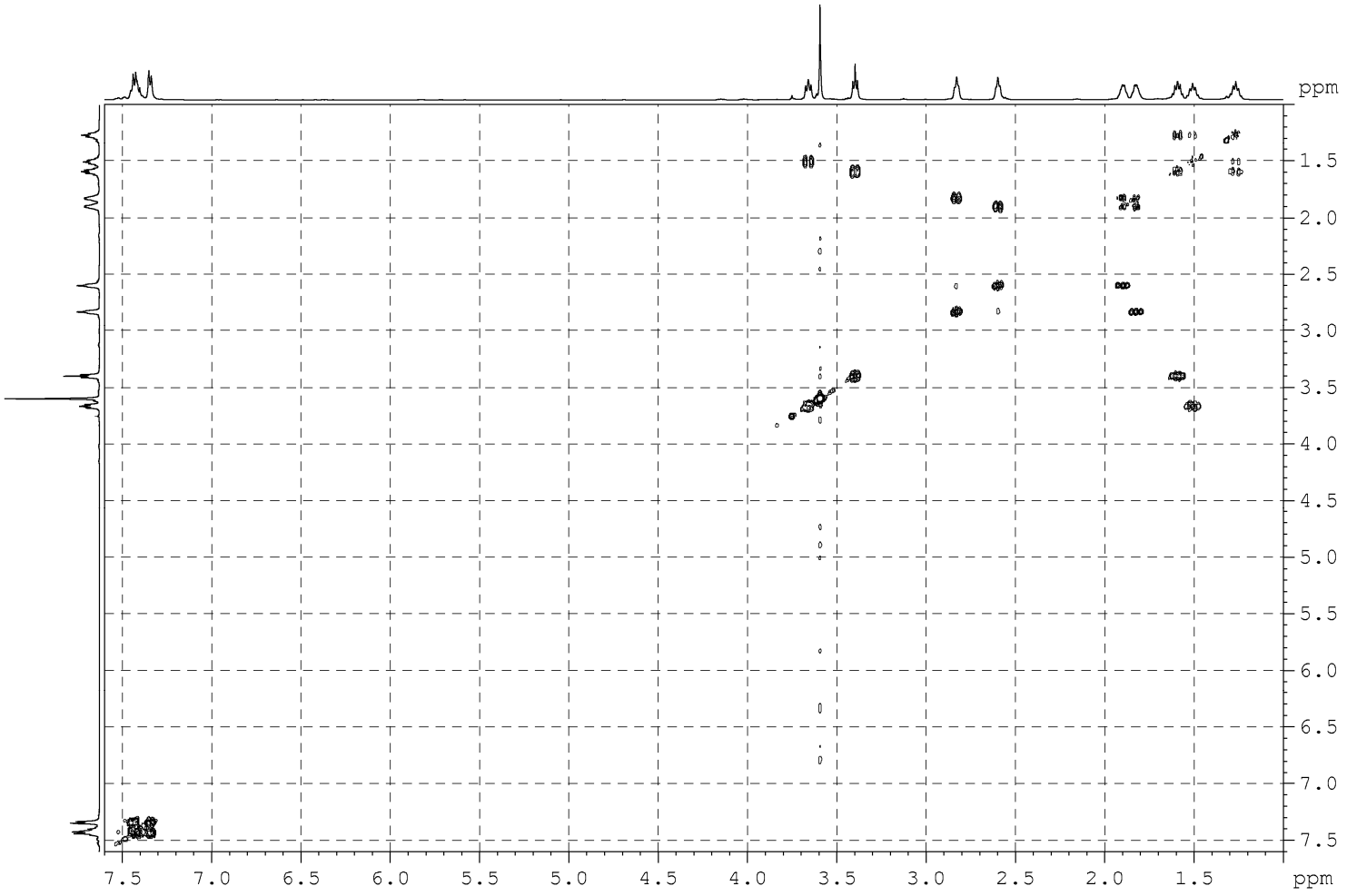

Figure S21. 2D ^{1}H-^{1}H COSY NMR spectra of **5a** in $CDCl_3$ at T = 303 K.

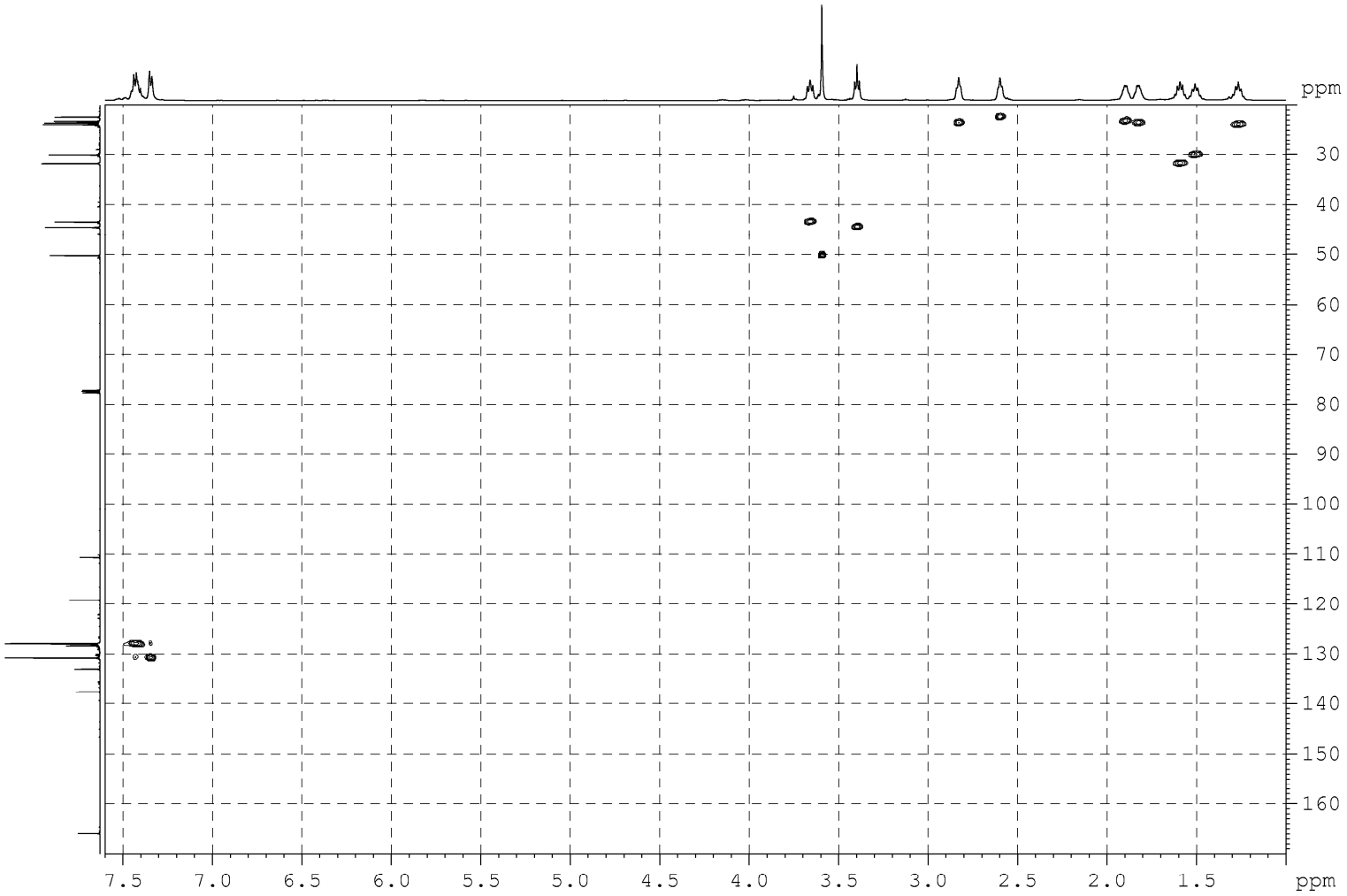

Figure S22. 2D ^{1}H-^{13}C HSQC NMR spectra of **5a** in $CDCl_3$ at T = 303 K.

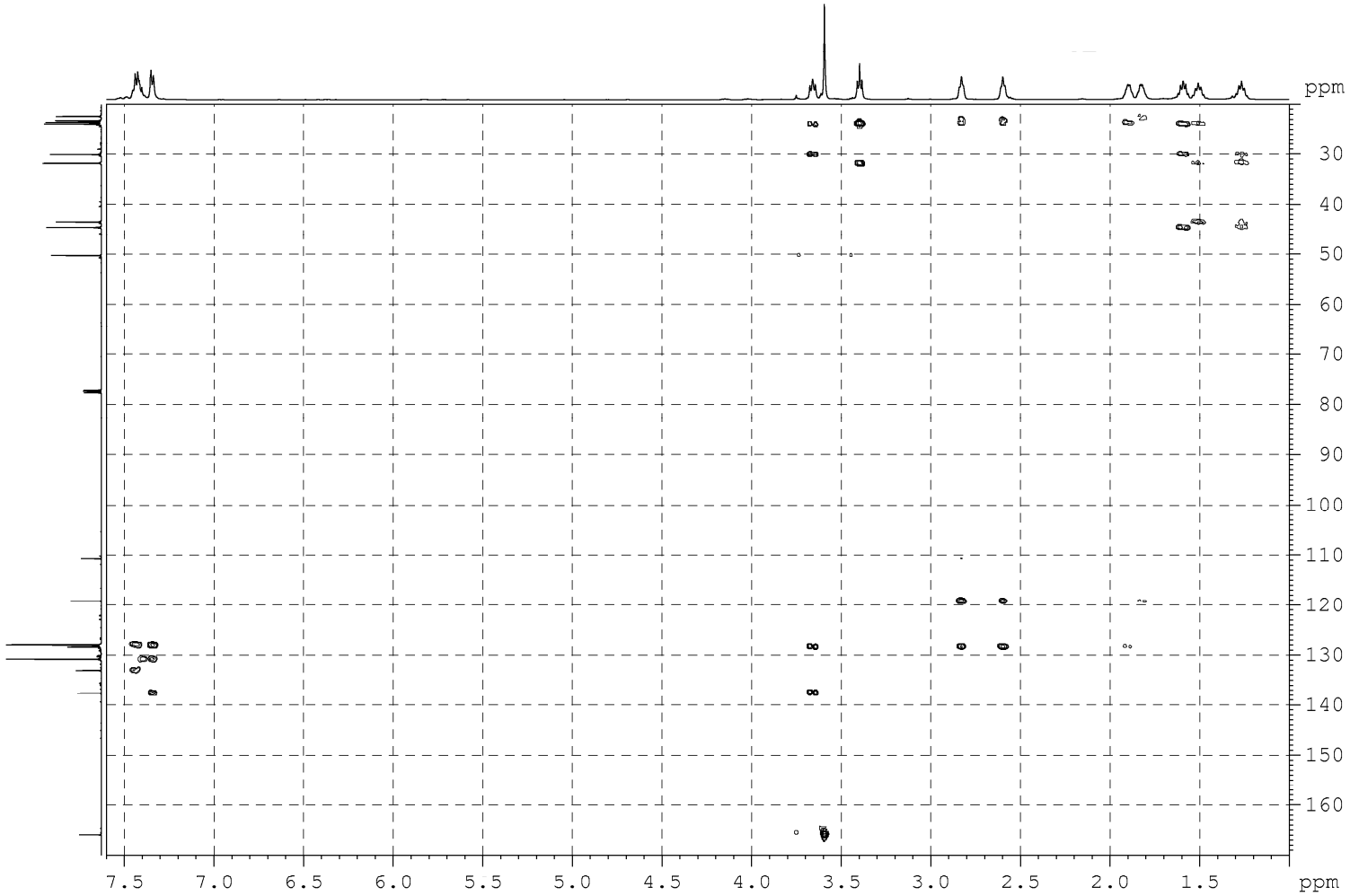

Figure S23. 2D ^{1}H-^{13}C HMBC NMR spectra of **5a** in $CDCl_3$ at T = 303 K.

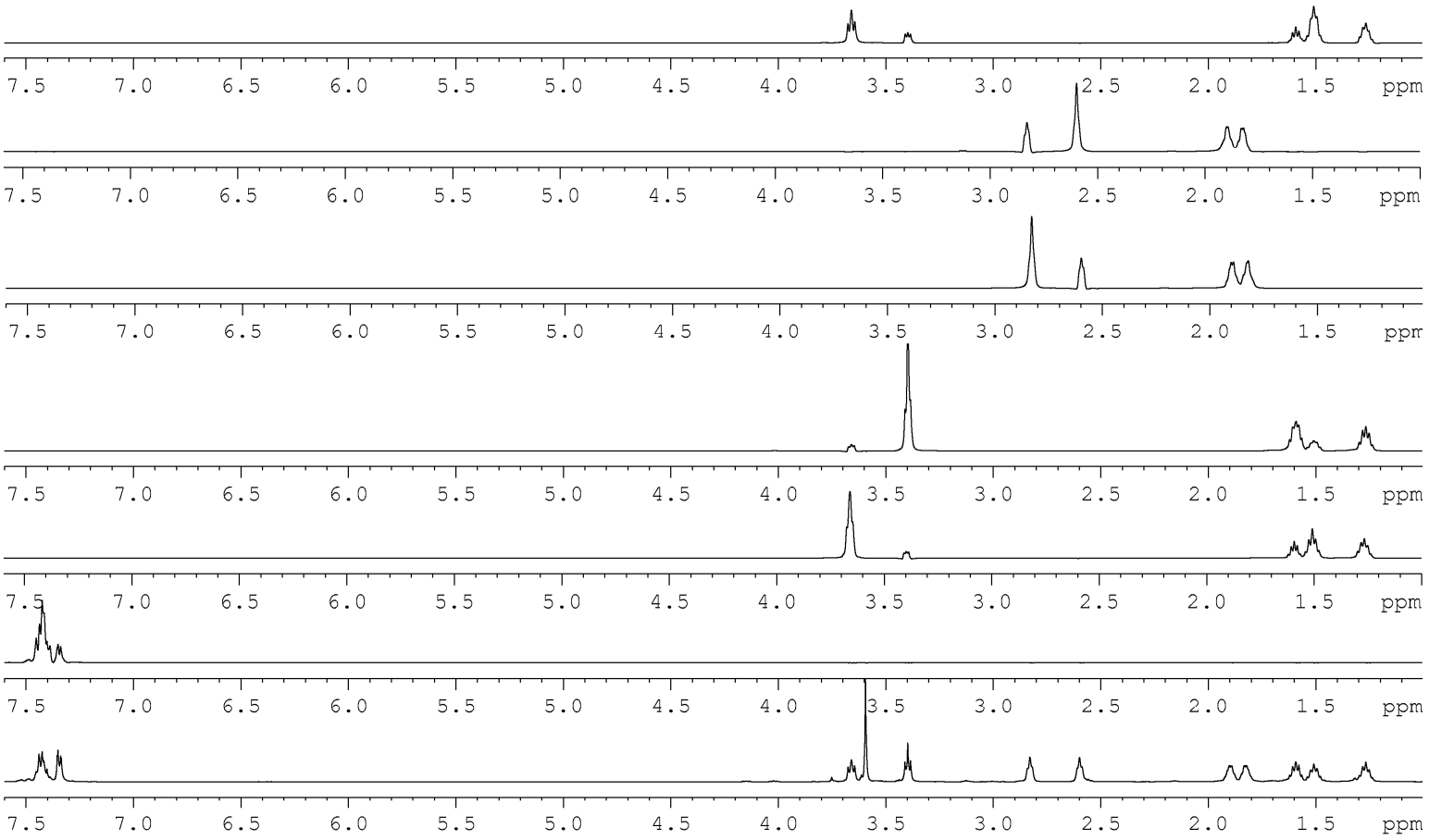

Figure S24. 1D ^{1}H and ^{1}H TOCSY NMR spectra of **5a** in $CDCl_3$ at T = 303 K.

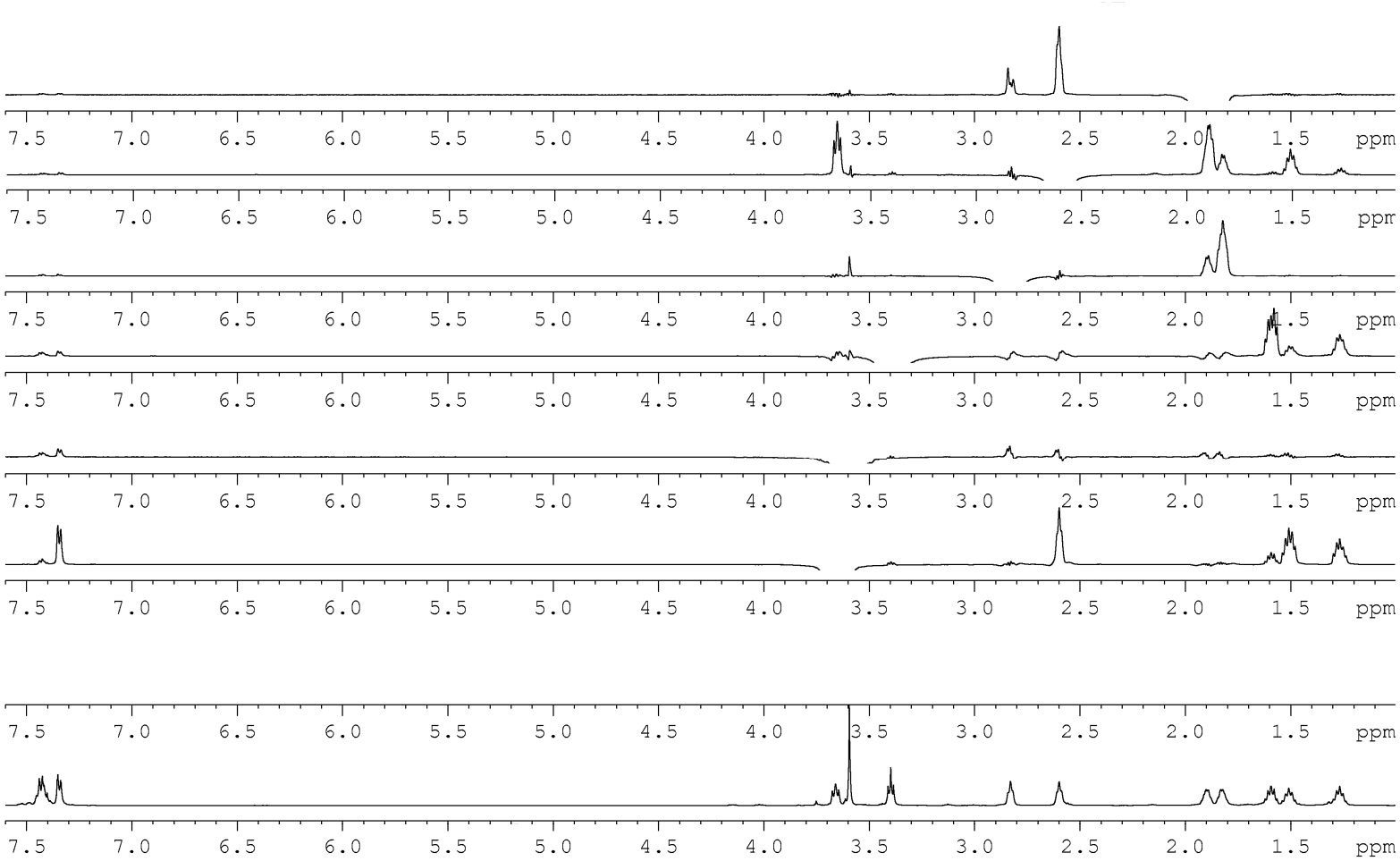

Figure S25. 1D ^{1}H and ^{1}H DPFGROE NMR spectra of **5a** in $CDCl_3$ at T = 303 K.

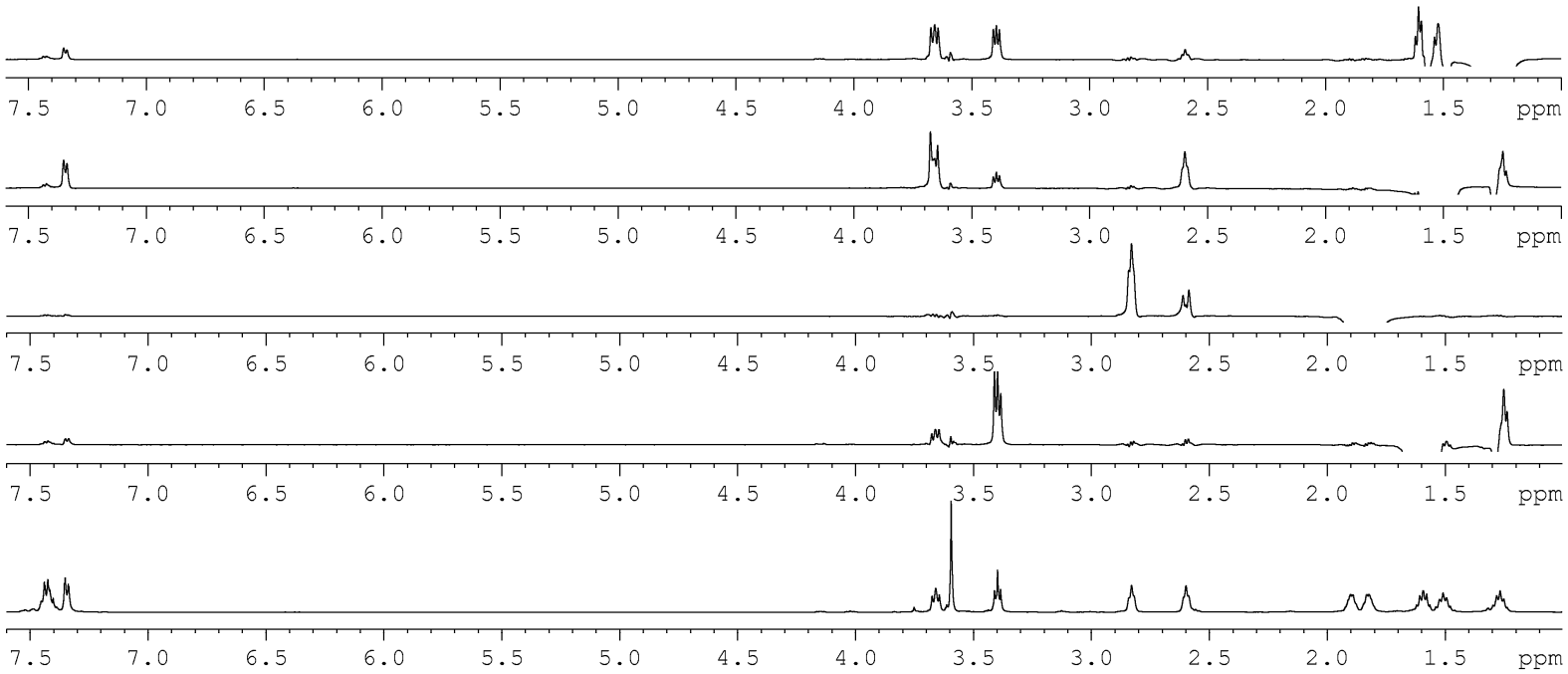

Figure S26. 1D ^{1}H and ^{1}H DPFGROE NMR spectra of **5a** in $CDCl_3$ at T = 303 K.

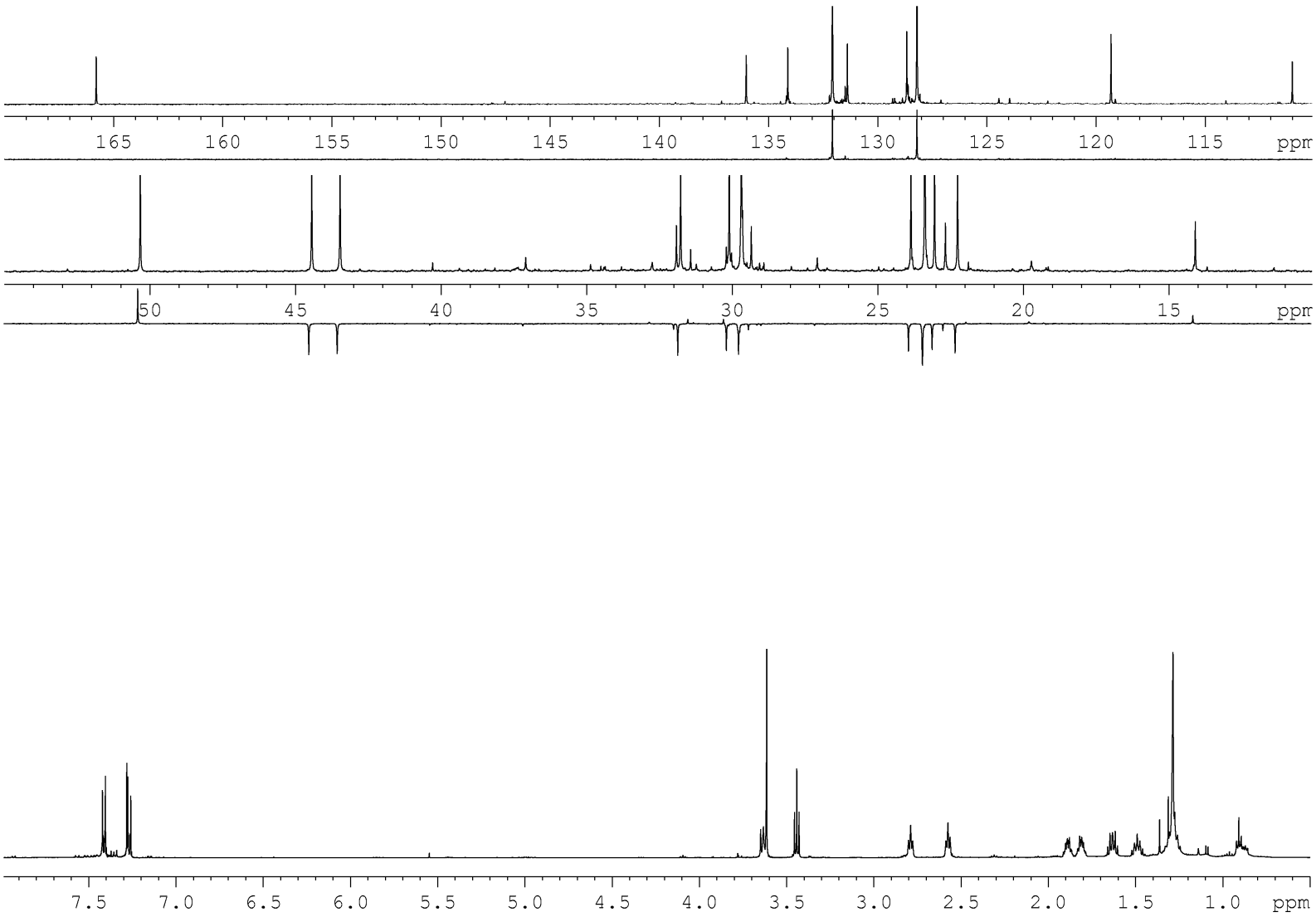

Figure S27. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **5b** in $CDCl_3$ at T = 303 K.

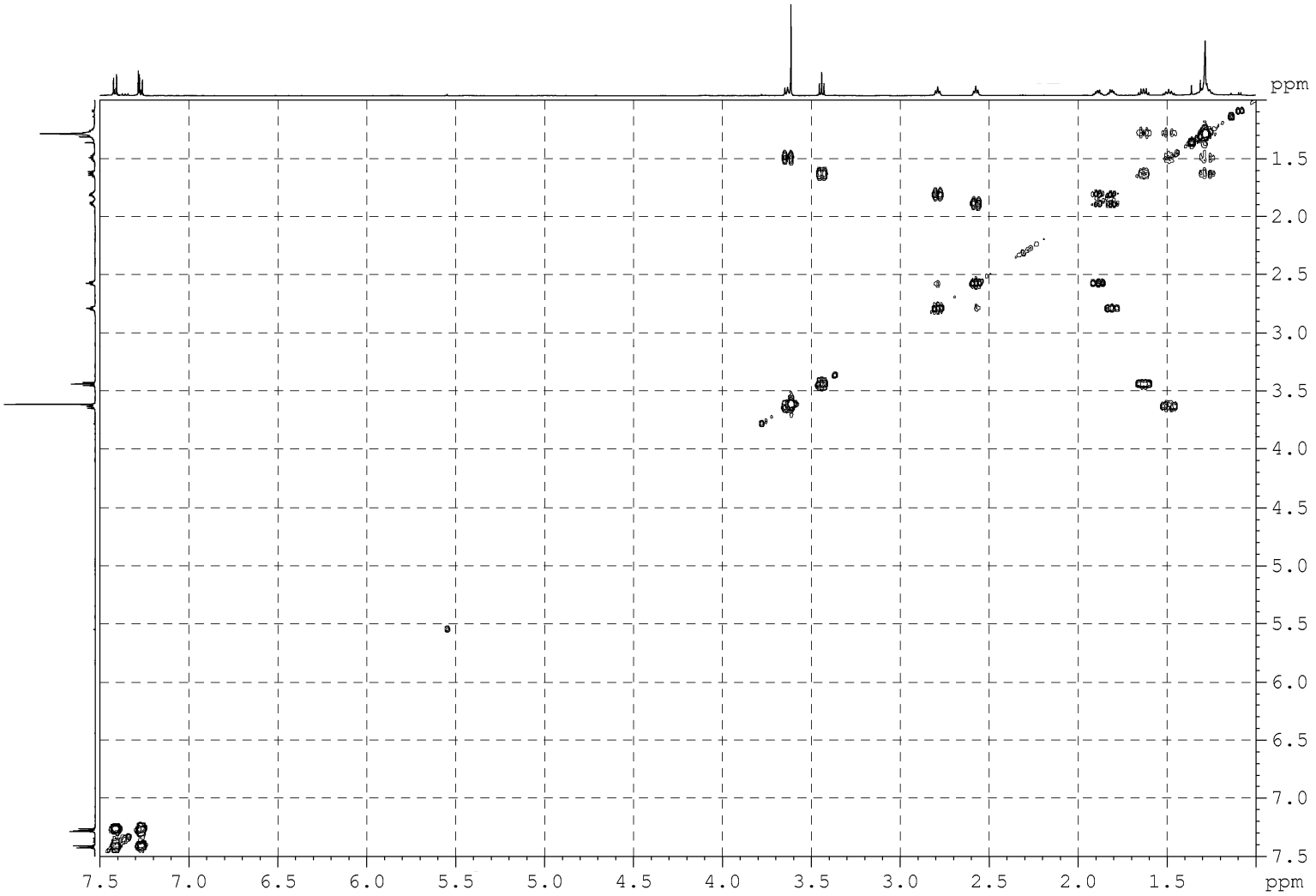

Figure S28. 2D ^{1}H-^{1}H COSY NMR spectra of **5b** in $CDCl_3$ at T = 303 K.

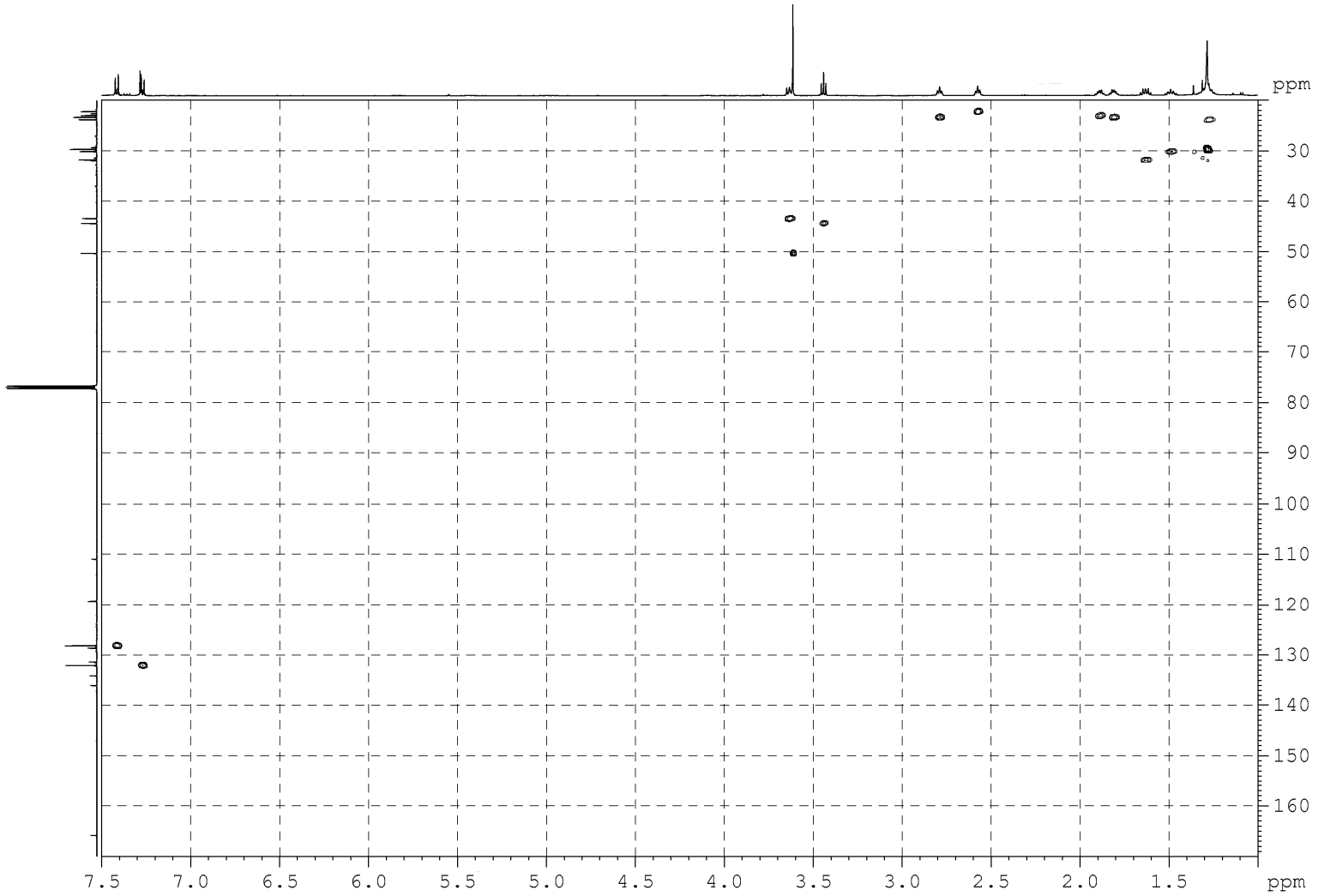

Figure S29. 2D ^{1}H-^{13}C HSQC NMR spectra of **5b** in $CDCl_3$ at T = 303 K.

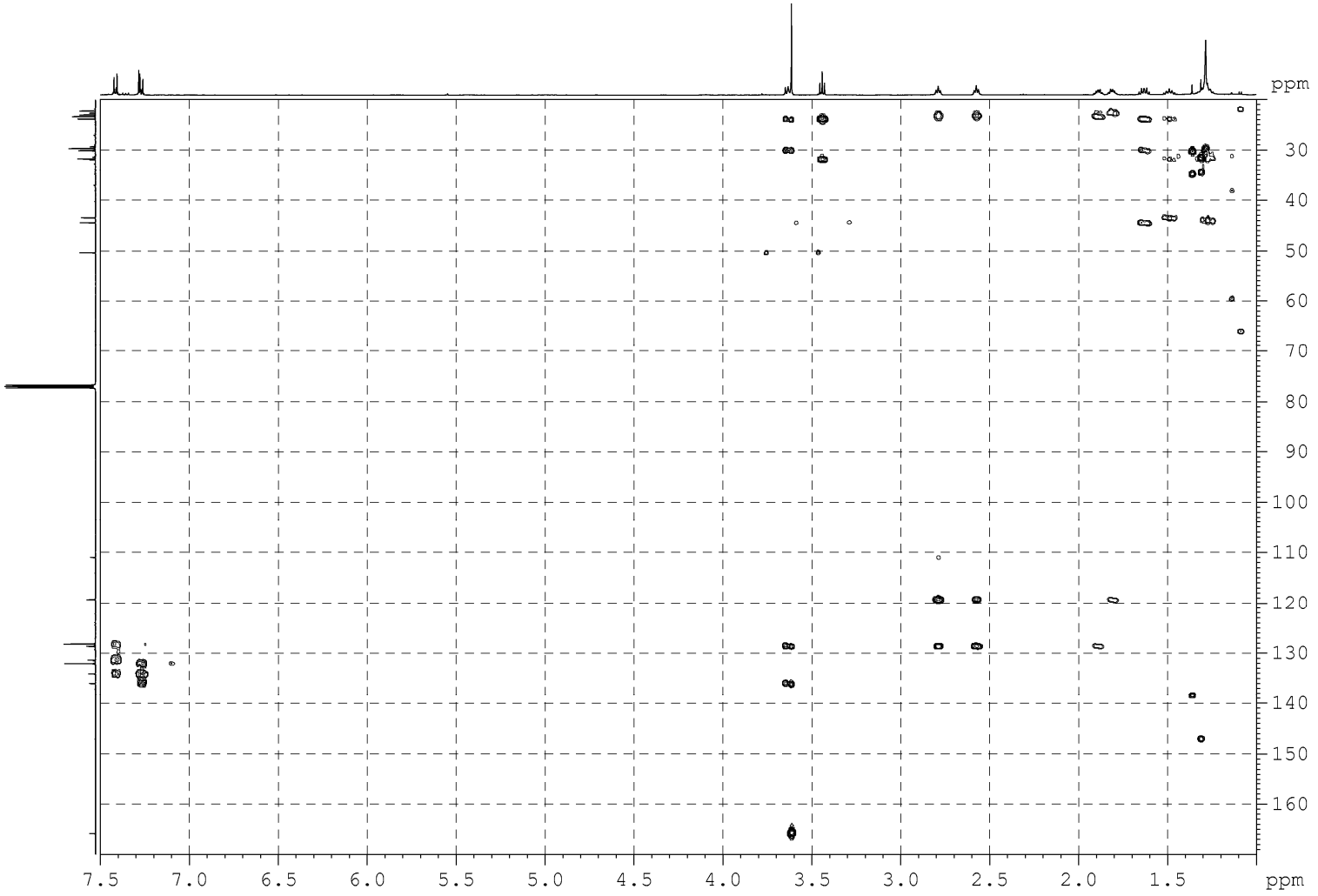

Figure S30. 2D ^{1}H-^{13}C HMBC NMR spectra of **5b** in $CDCl_3$ at T = 303 K.

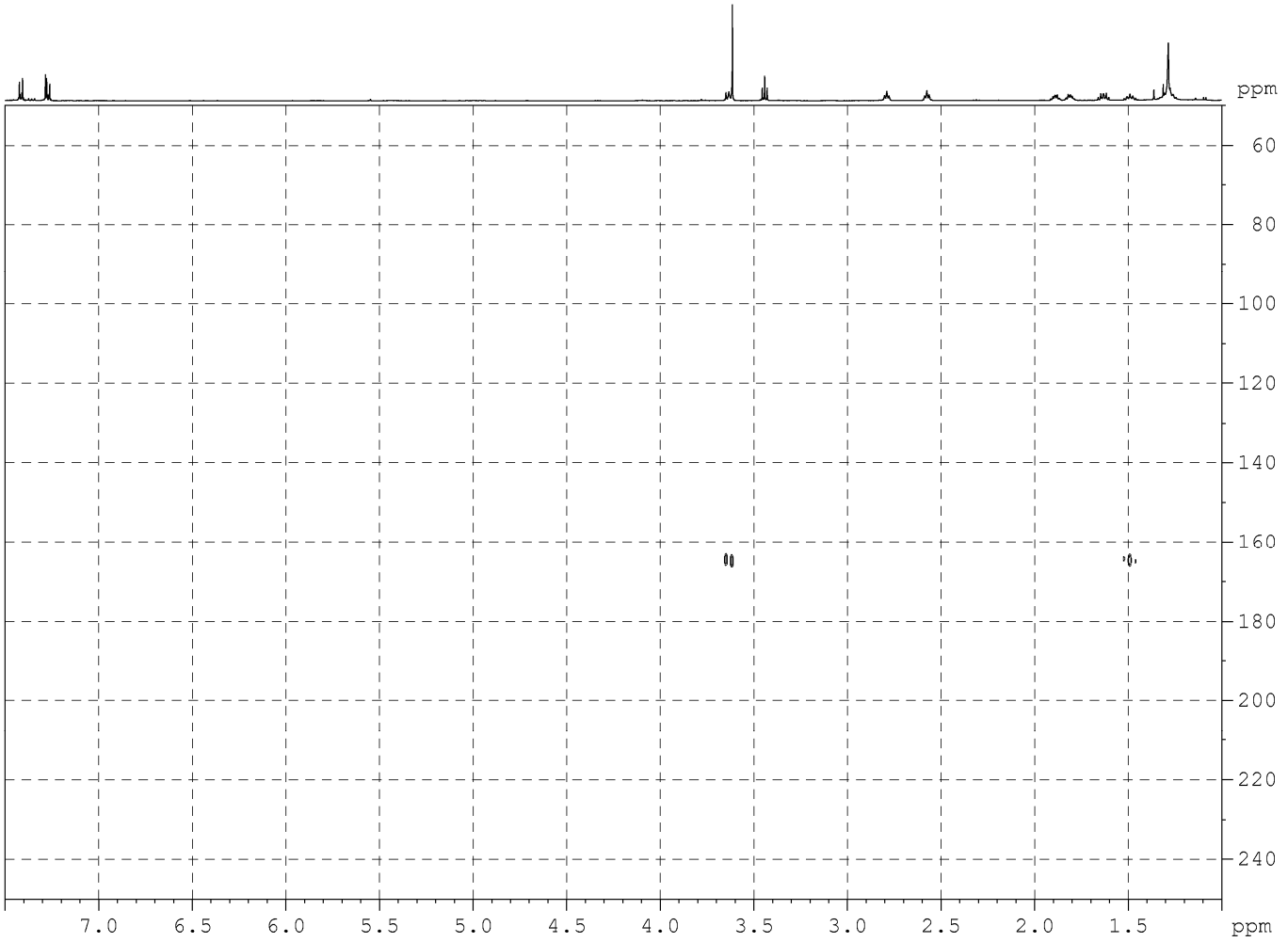

Figure S31. 2D ^{1}H-^{15}N HMBC NMR spectra of **5b** in $CDCl_3$ at T = 303 K.

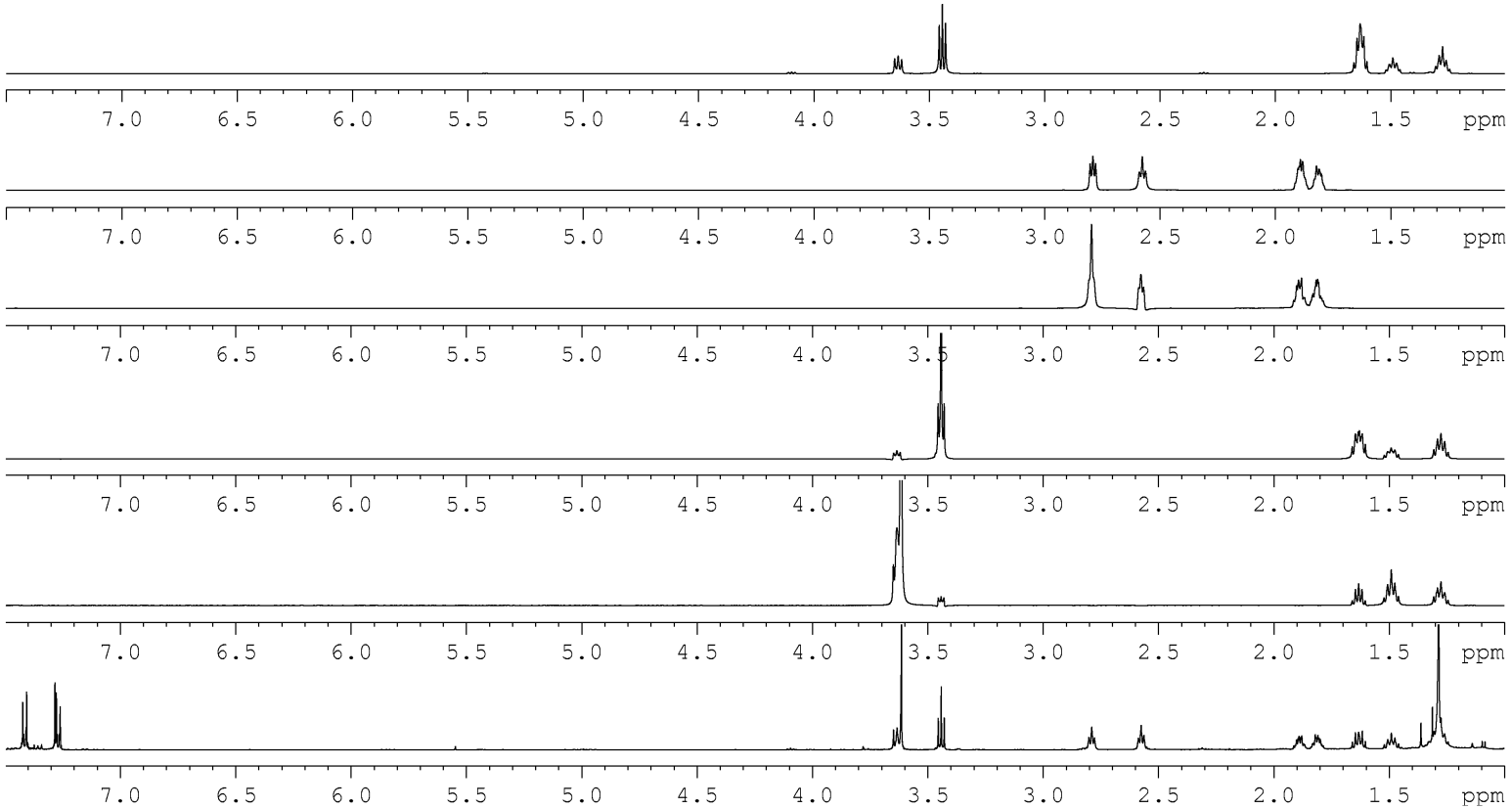

Figure S32. 1D ^{1}H and ^{1}H TOCSY NMR spectra of **5b** in $CDCl_3$ at T = 303 K.

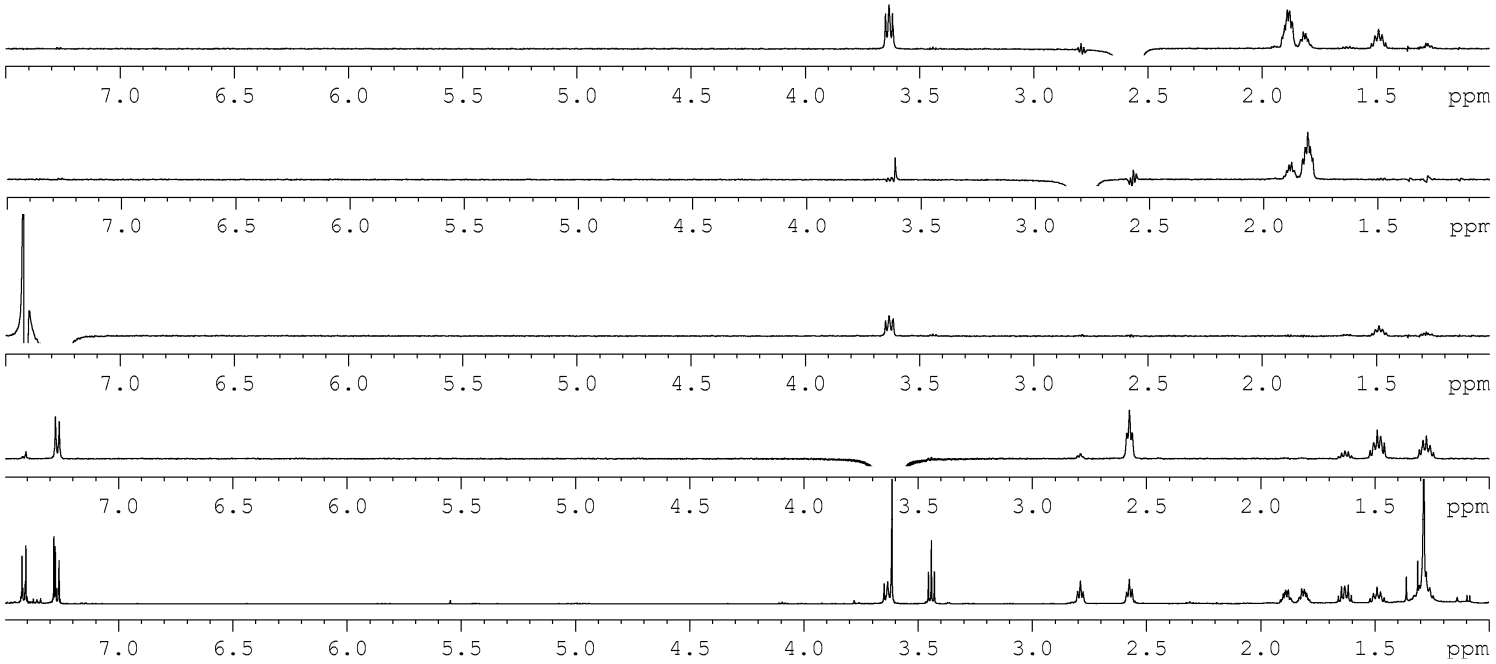

Figure S33. 1D ^{1}H and ^{1}H DPFGROE NMR spectra of **5b** in $CDCl_3$ at T = 303 K.

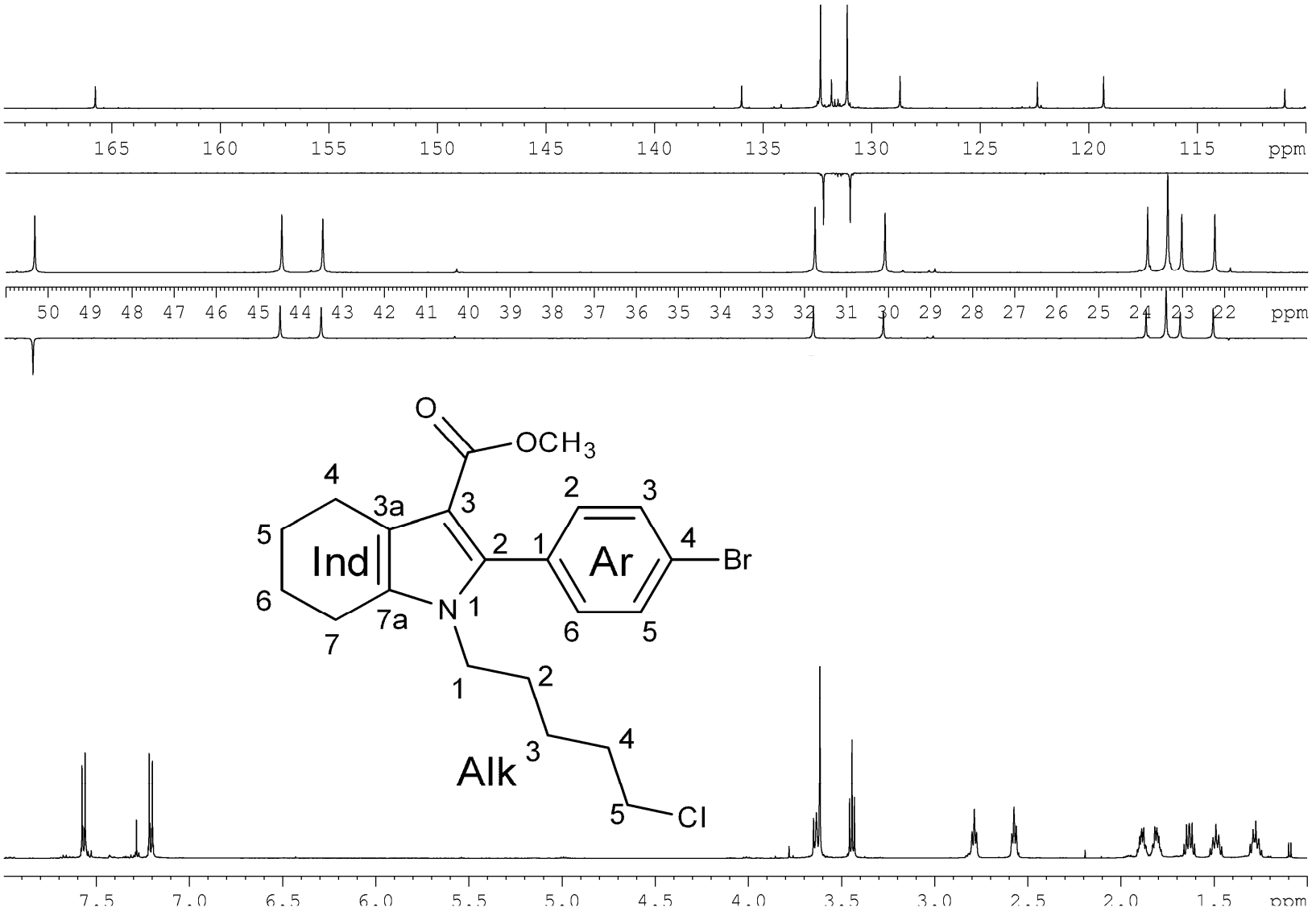

Figure S34. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **5c** in $CDCl_3$ at T = 303 K.

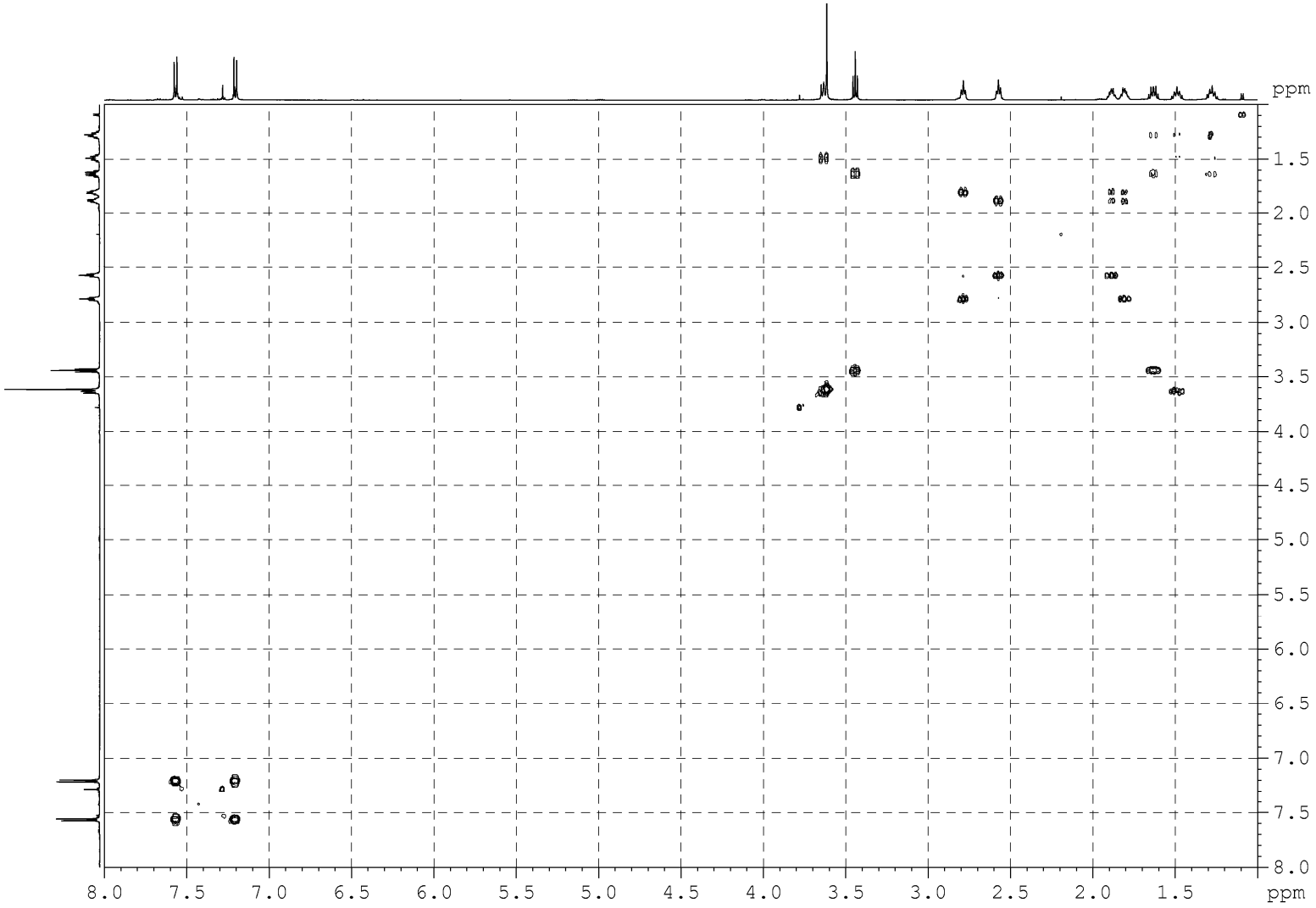

Figure S35. 2D ^{1}H-^{1}H COSY NMR spectra of **5c** in $CDCl_3$ at T = 303 K.

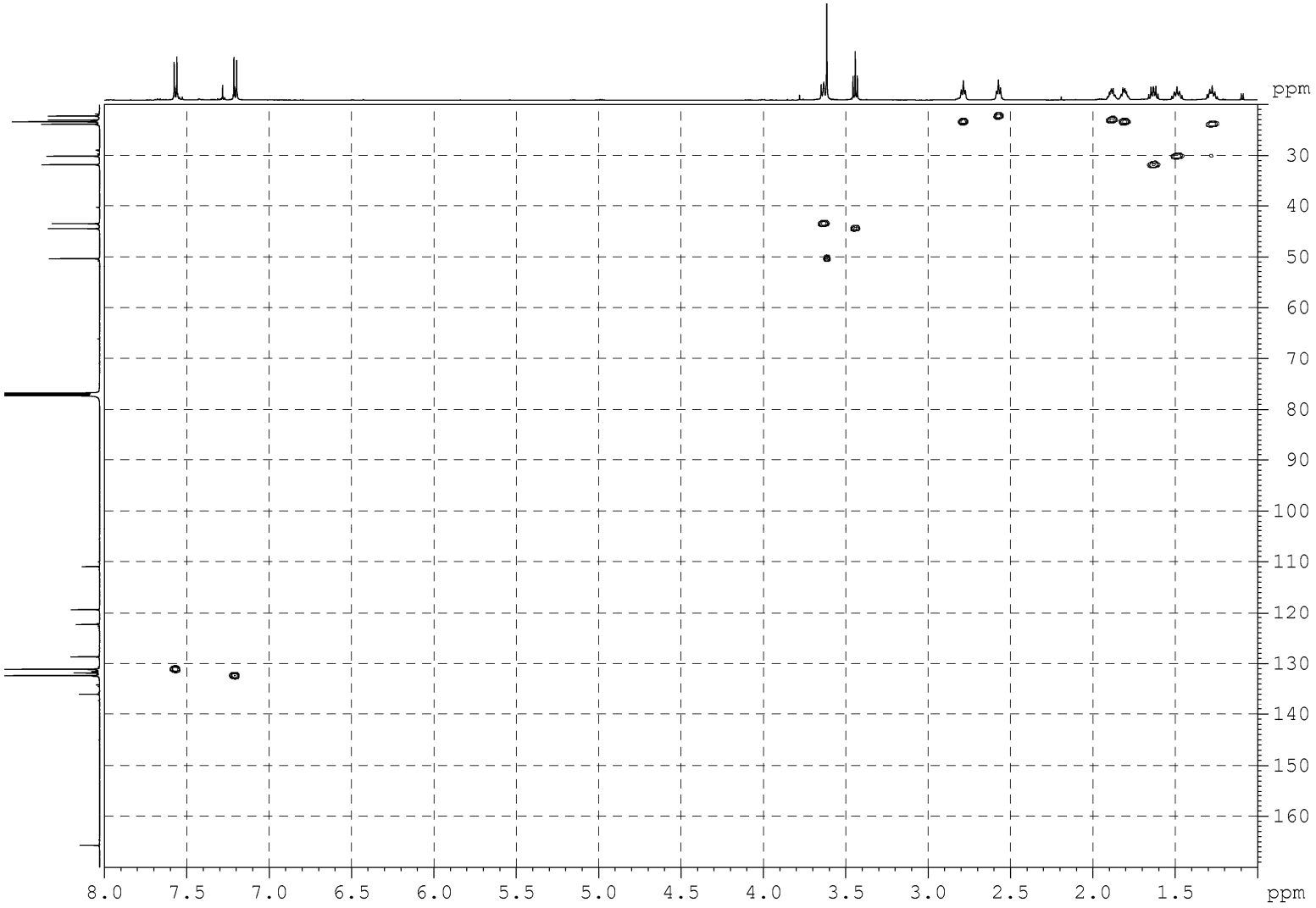

Figure S36. 2D ^{1}H-^{13}C HSQC NMR spectra of **5c** in $CDCl_3$ at T = 303 K.

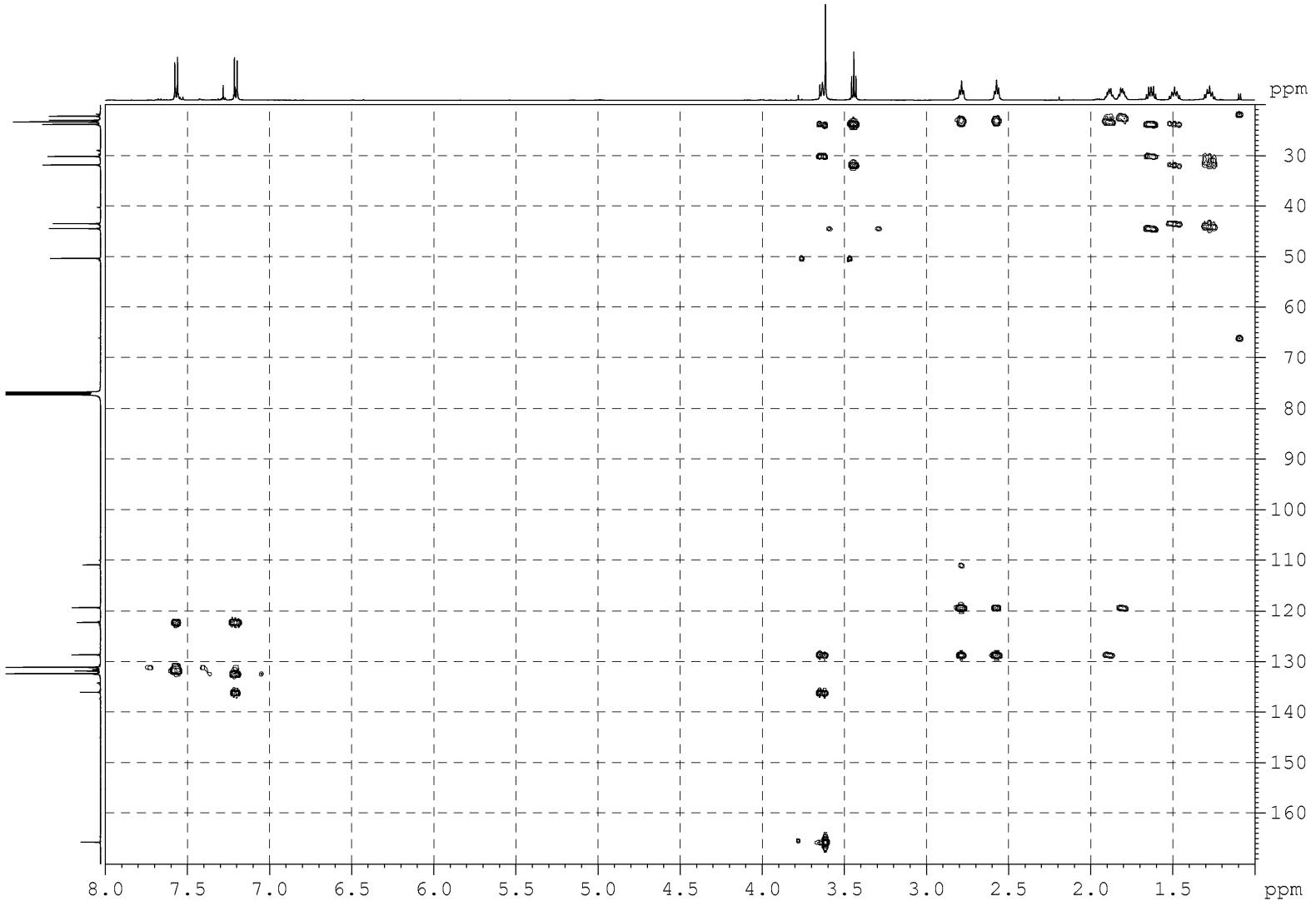

Figure S37. 2D ^{1}H-^{13}C HMBC NMR spectra of **5c** in $CDCl_3$ at T = 303 K.

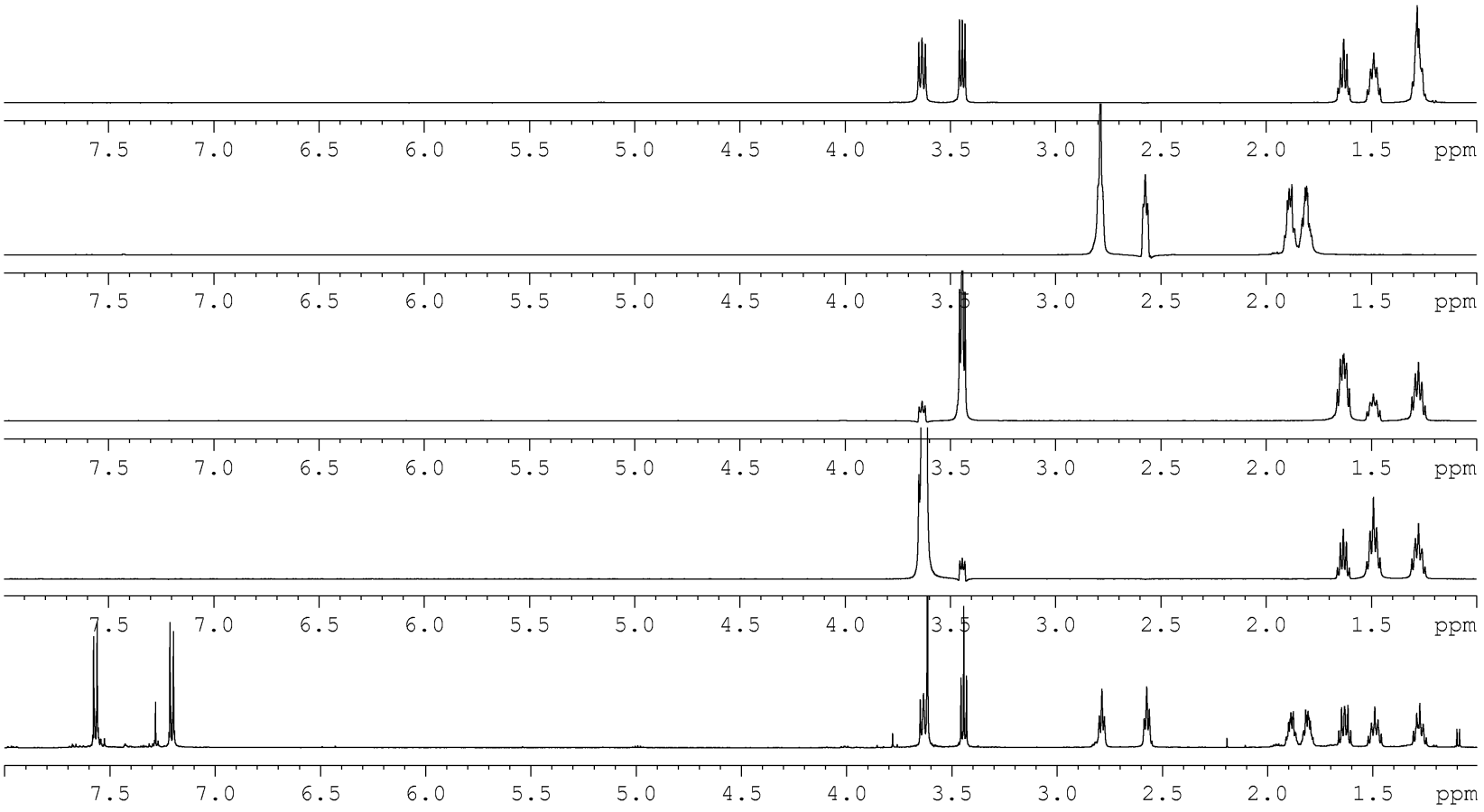

Figure S38. 1D ^{1}H and ^{1}H TOCSY NMR spectra of **5c** in $CDCl_3$ at T = 303 K.

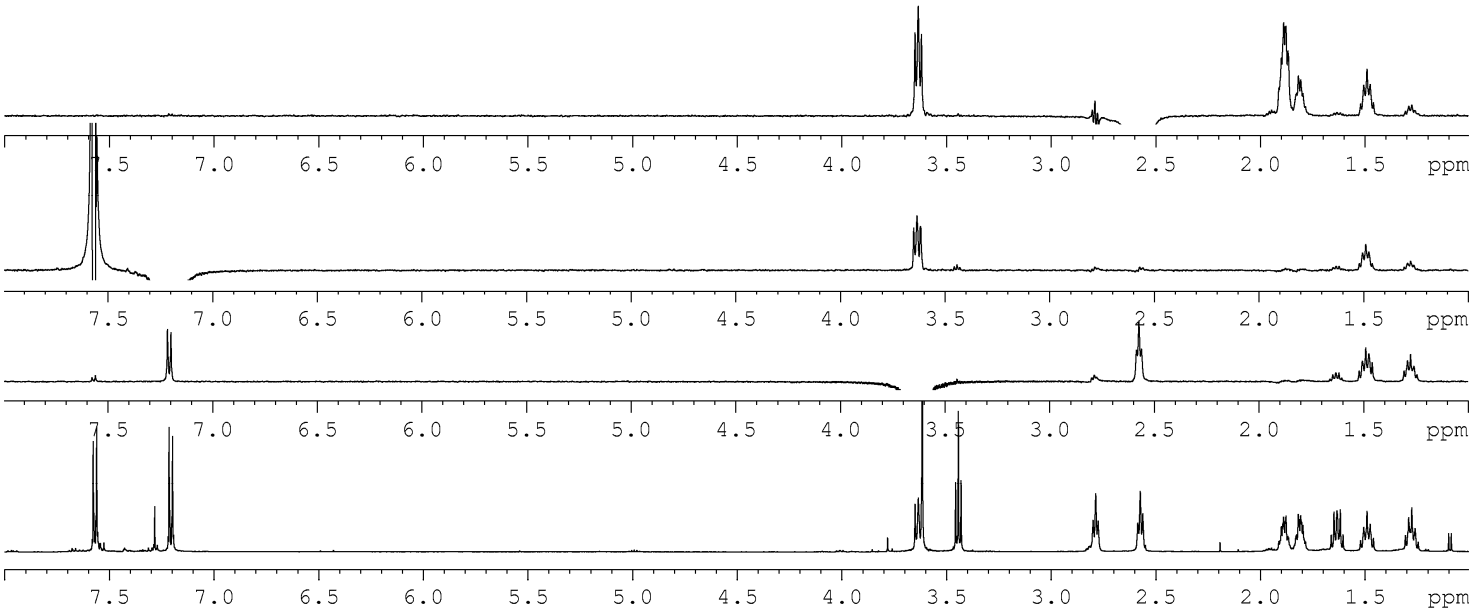

Figure S39. 1D ^{1}H and ^{1}H DPFGROE NMR spectra of **5c** in $CDCl_3$ at T = 303 K.

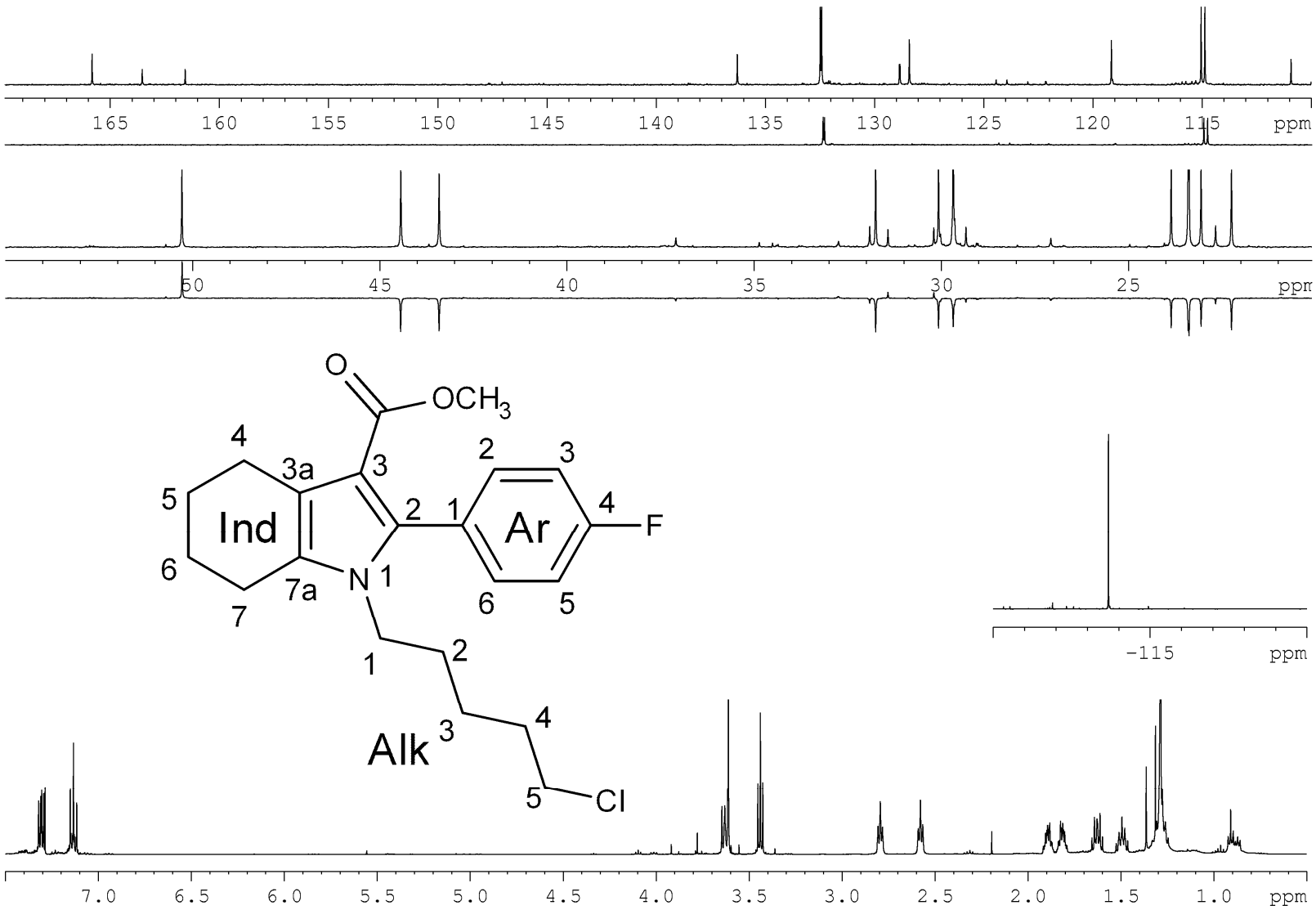

Figure S40. 1D ^{1}H, ^{13}C DEPT, $^{13}C\{^{1}H\}$ and $^{19}F\{^{1}H\}$ NMR spectra of **5d** in $CDCl_3$ at T = 303 K.

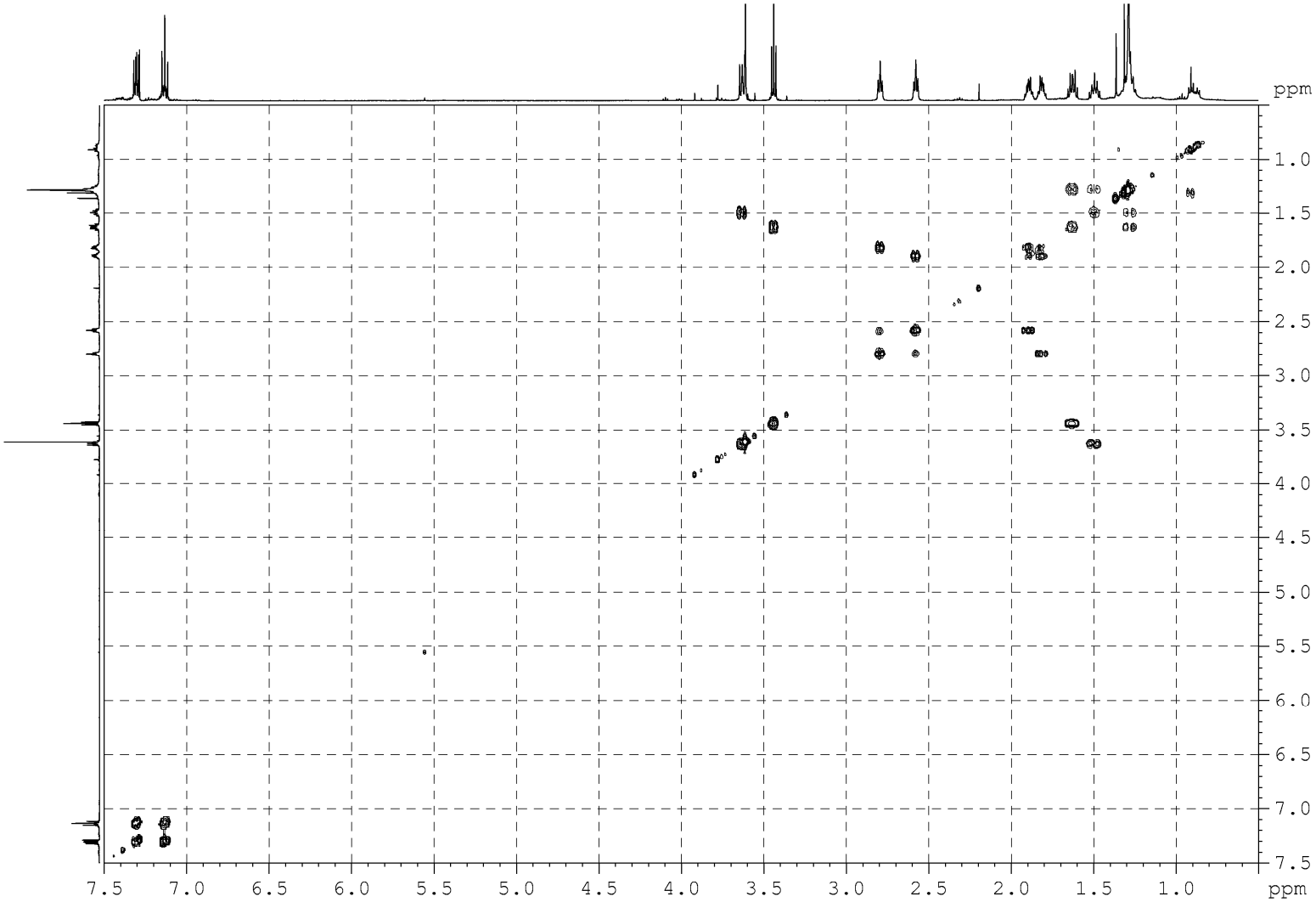

Figure S41. 2D ^{1}H-^{1}H COSY NMR spectra of **5d** in $CDCl_3$ at T = 303 K.

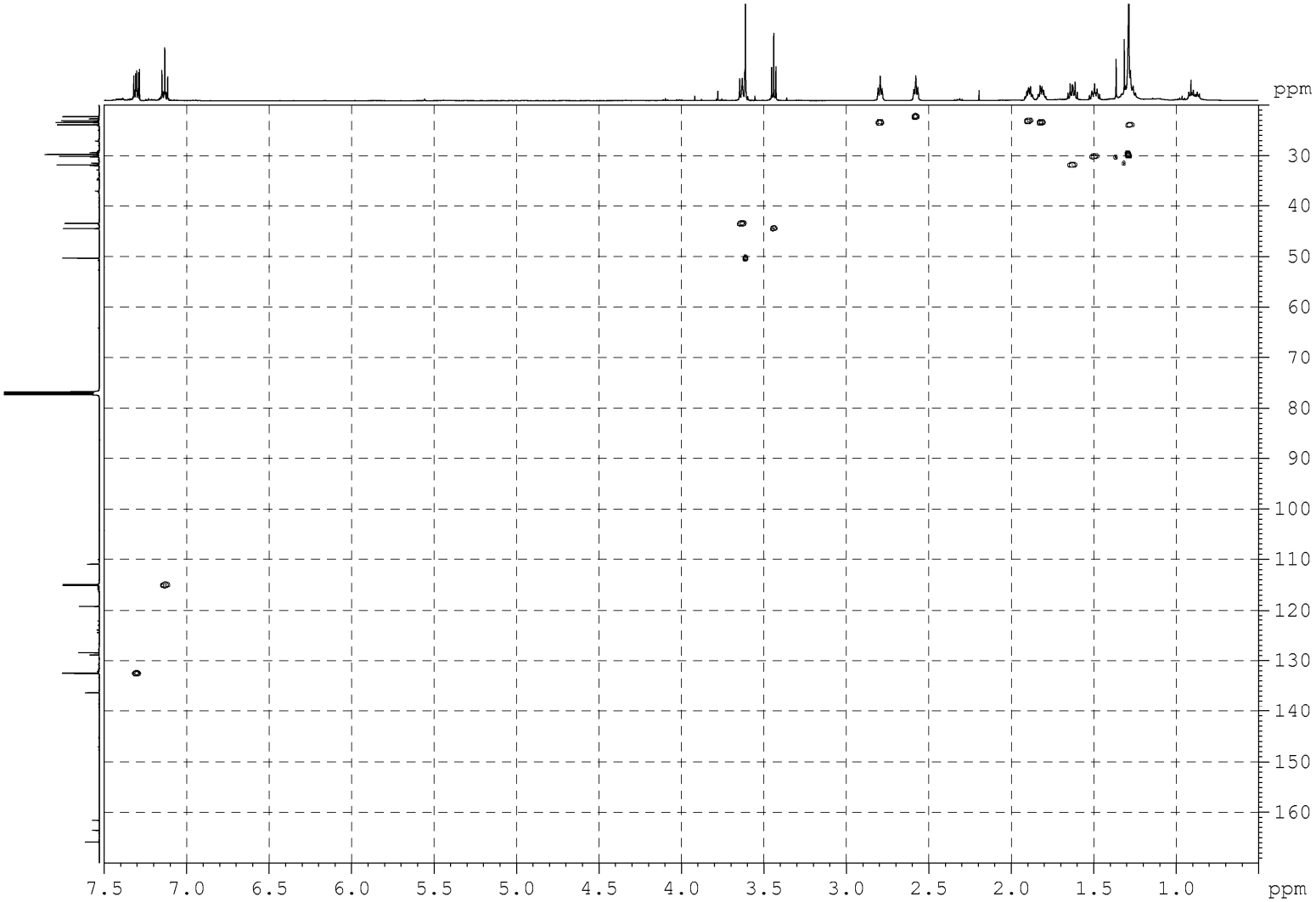

Figure S42. 2D ^{1}H-^{13}C HSQC NMR spectra of **5d** in $CDCl_3$ at T = 303 K.

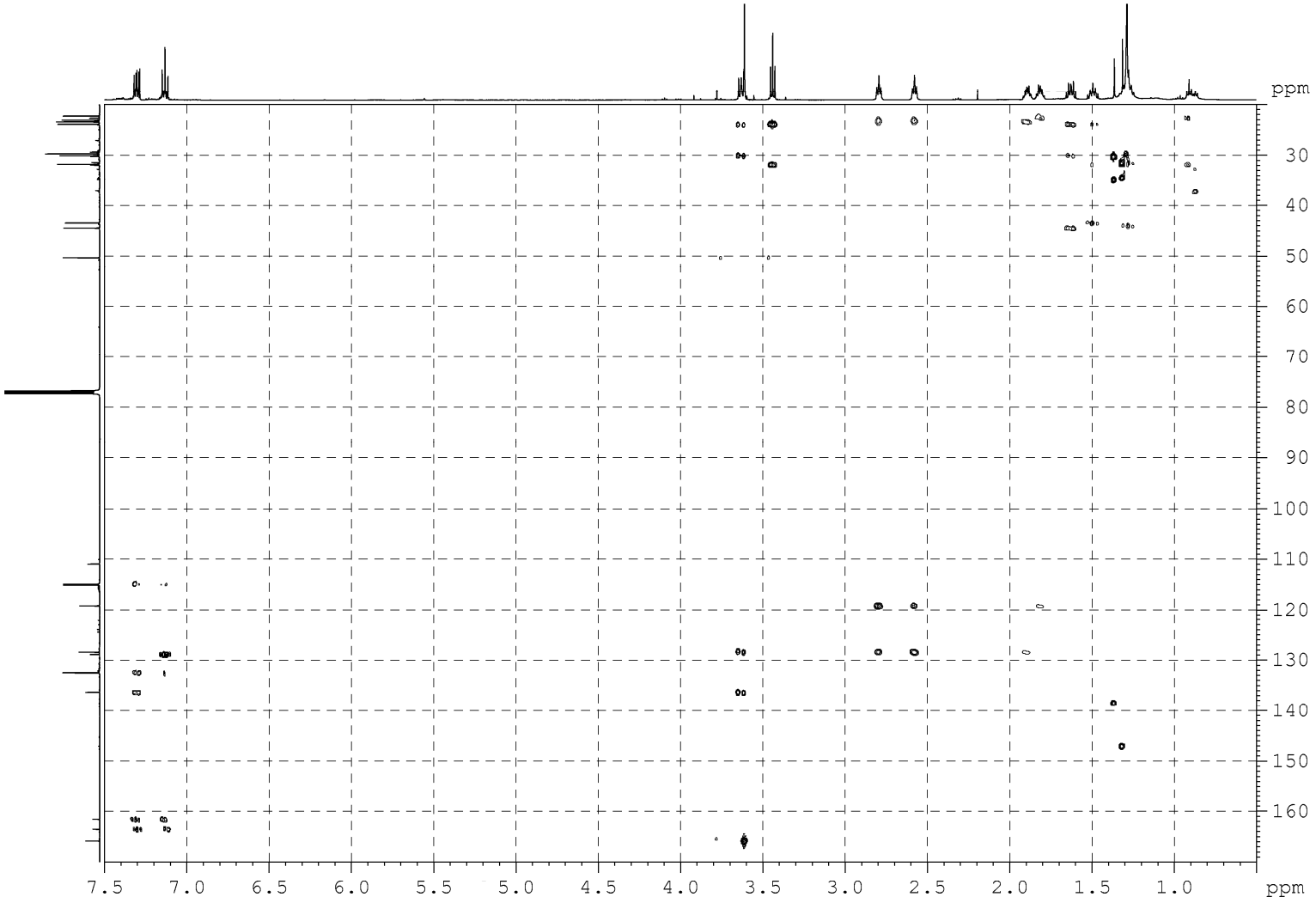

Figure S43. 2D ^{1}H-^{13}C HMBC NMR spectra of **5d** in $CDCl_3$ at T = 303 K.

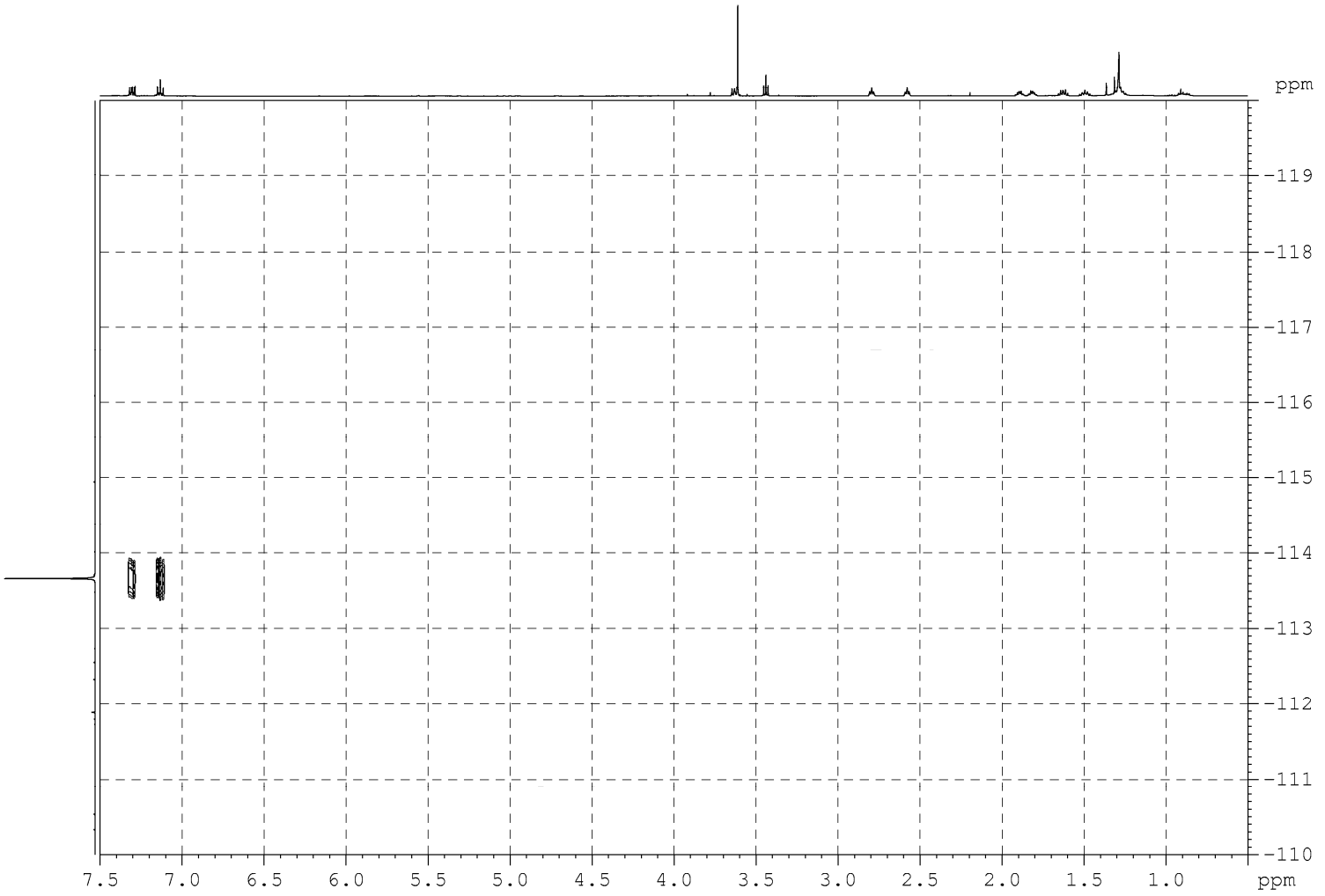

Figure S44. 2D ^{1}H-^{19}F HMBC NMR spectra of **5d** in $CDCl_3$ at T = 303 K.

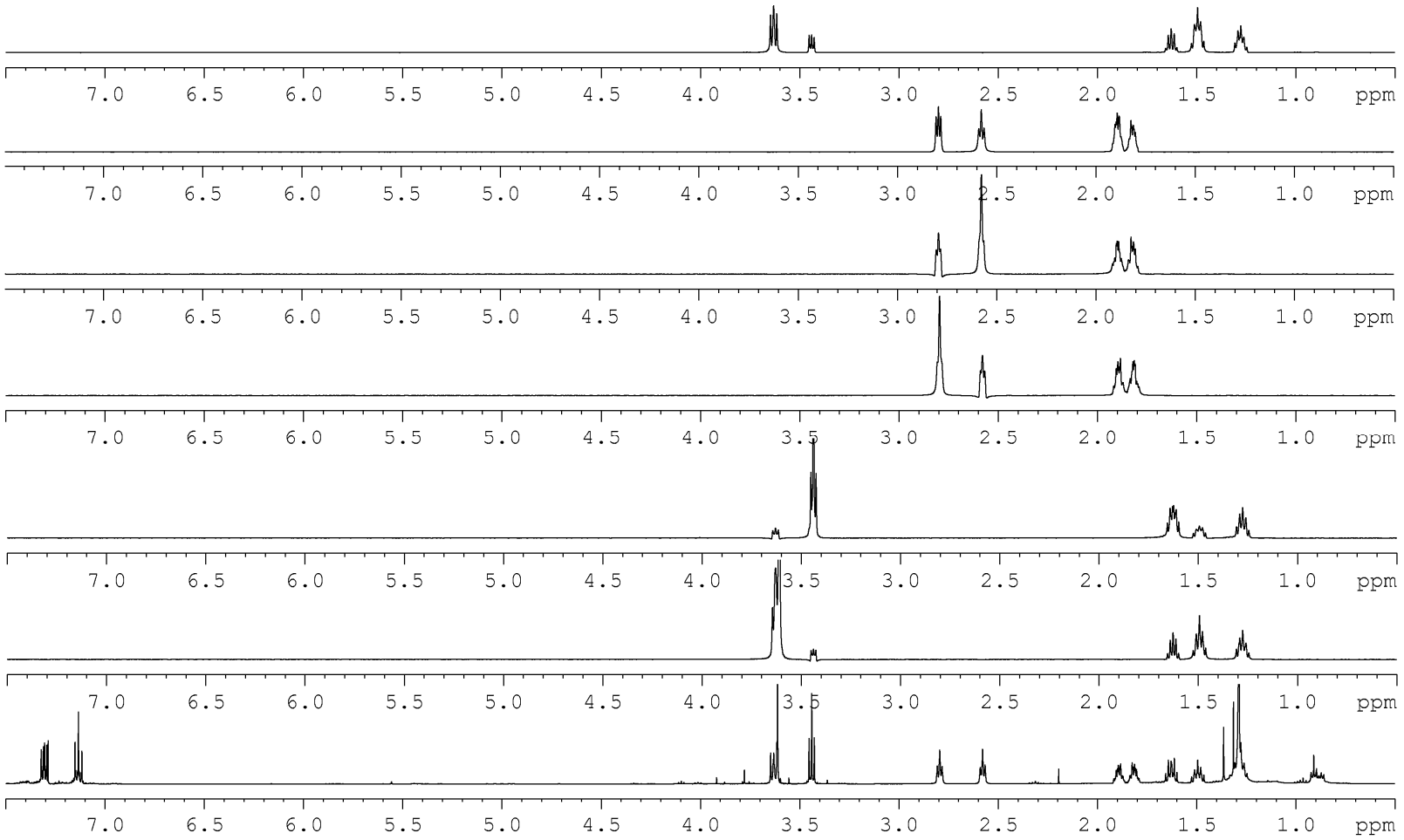

Figure S45. 1D ^{1}H and ^{1}H TOCSY NMR spectra of **5d** in $CDCl_3$ at T = 303 K.

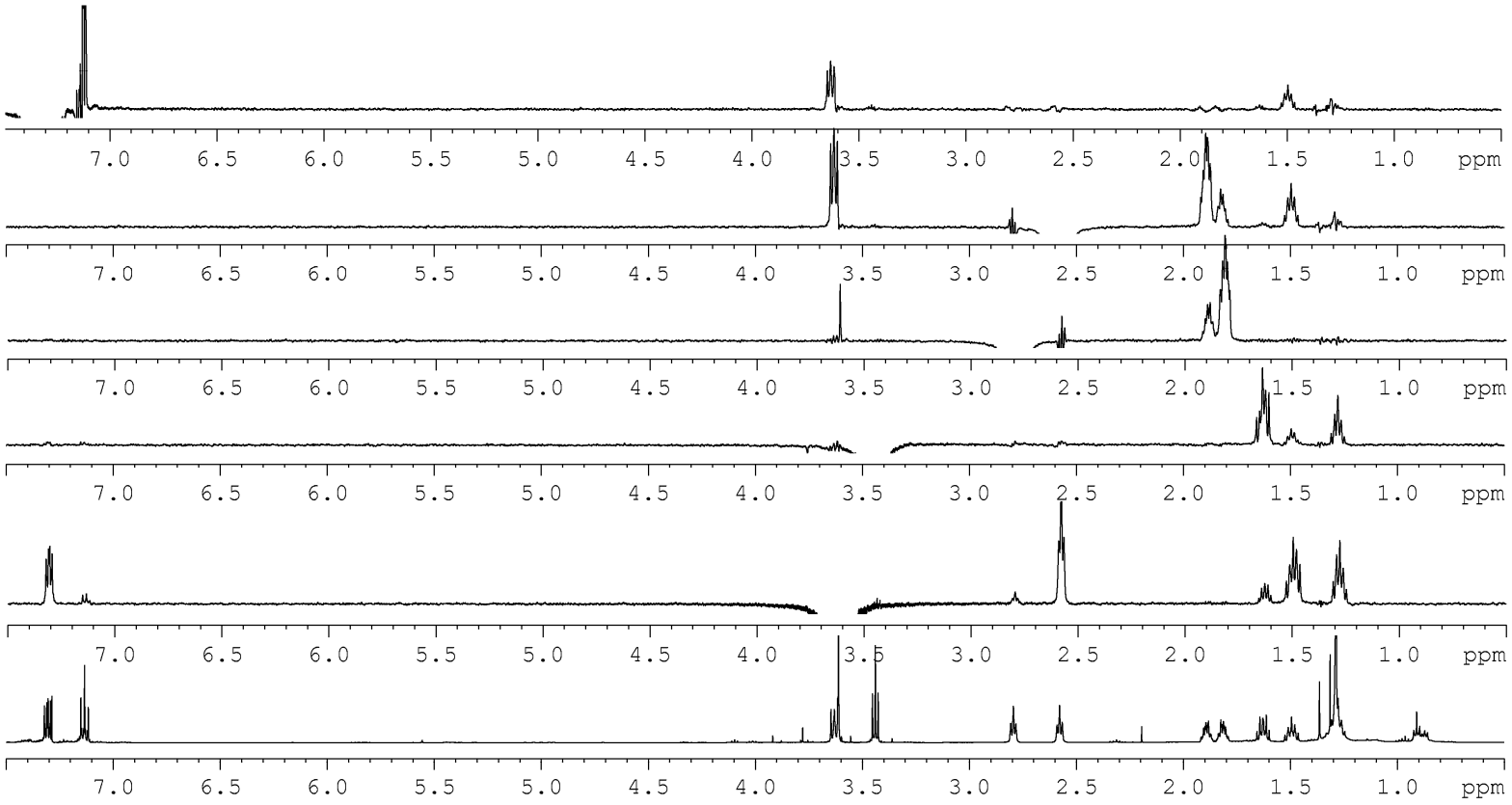

Figure S46. 1D ^{1}H and ^{1}H DPFGROE NMR spectra of **5d** in $CDCl_3$ at T = 303 K.

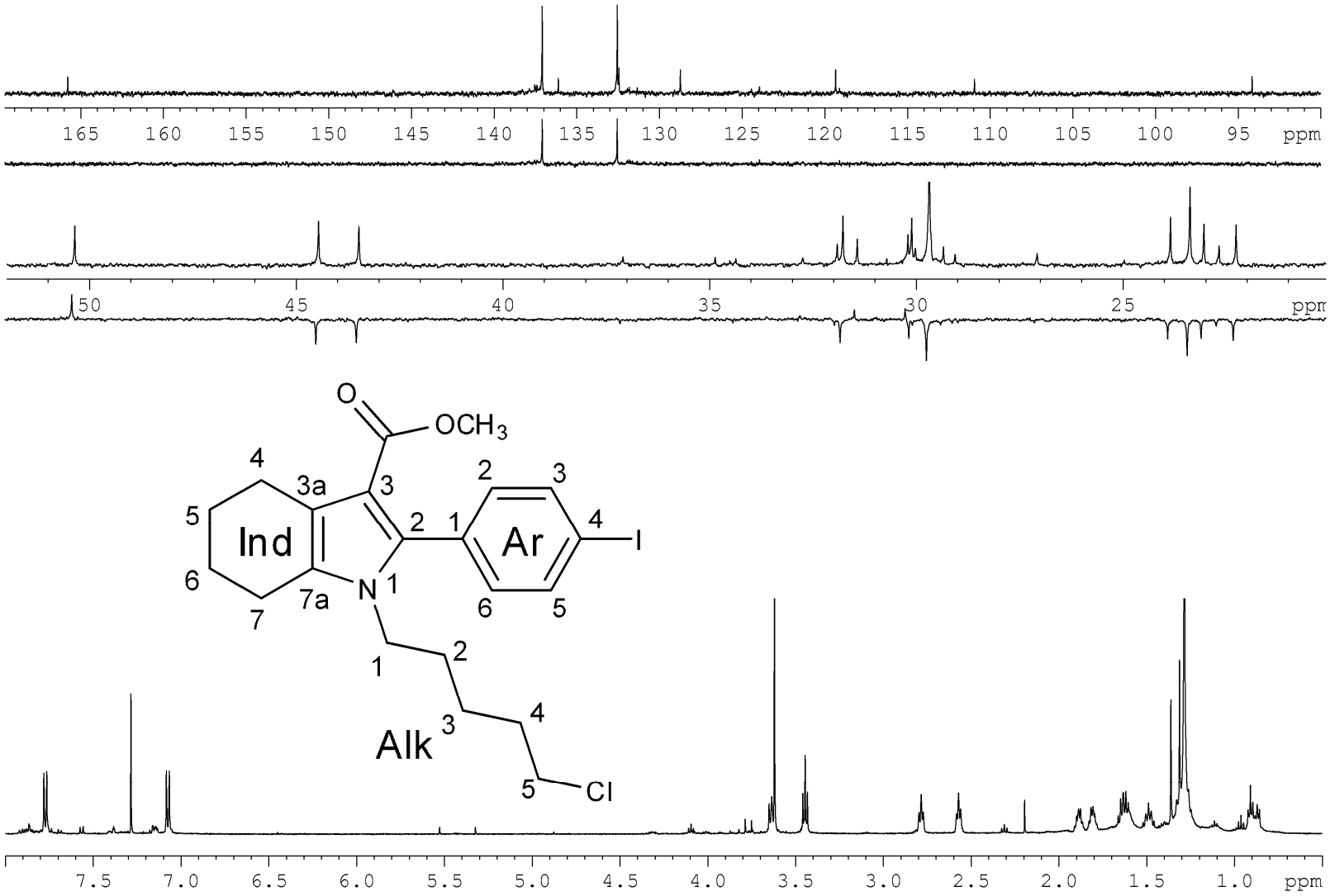

Figure S47. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **5e** in $CDCl_3$ at T = 303 K.

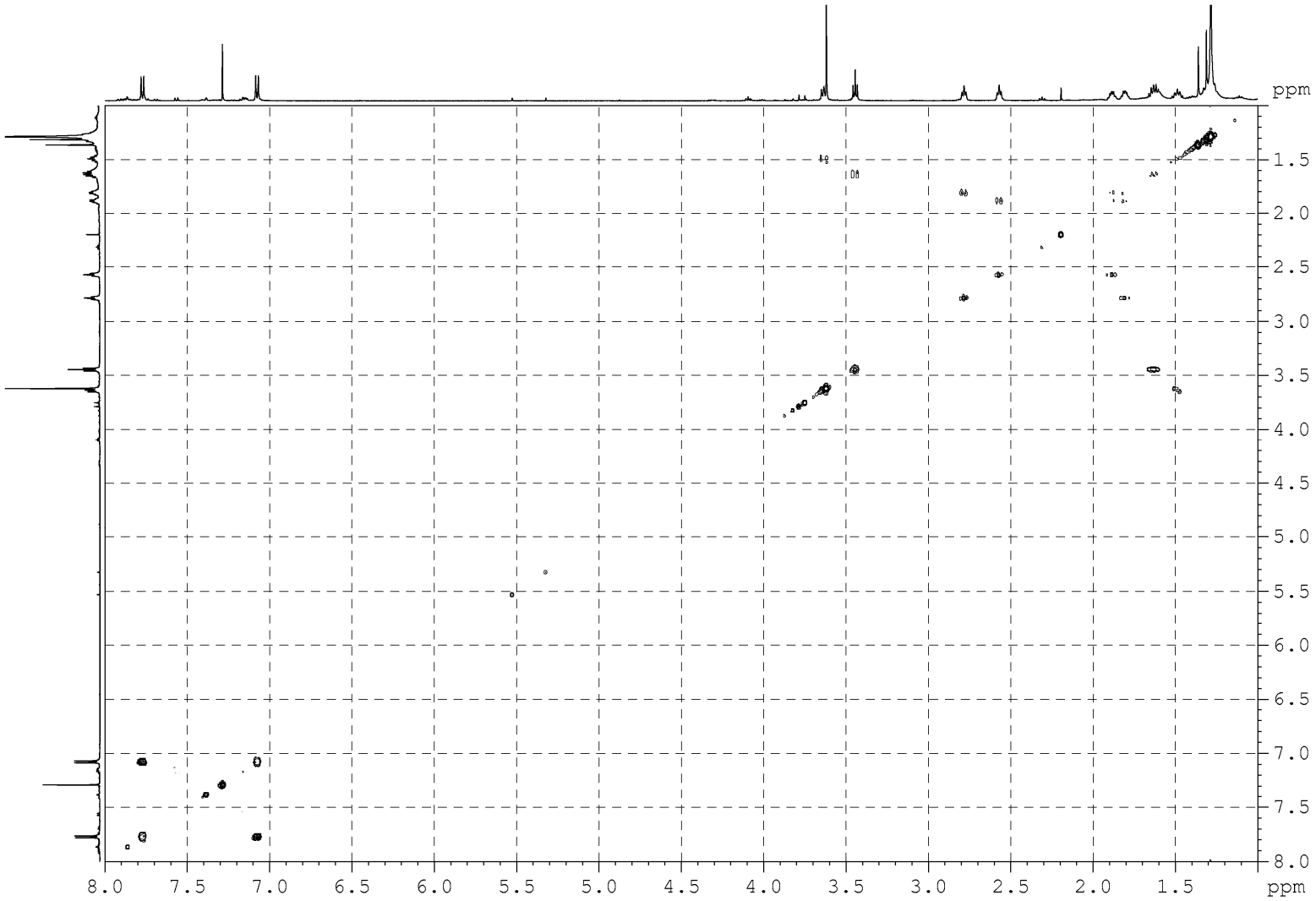

Figure S48. 2D ^{1}H-^{1}H COSY NMR spectra of **5e** in $CDCl_3$ at T = 303 K.

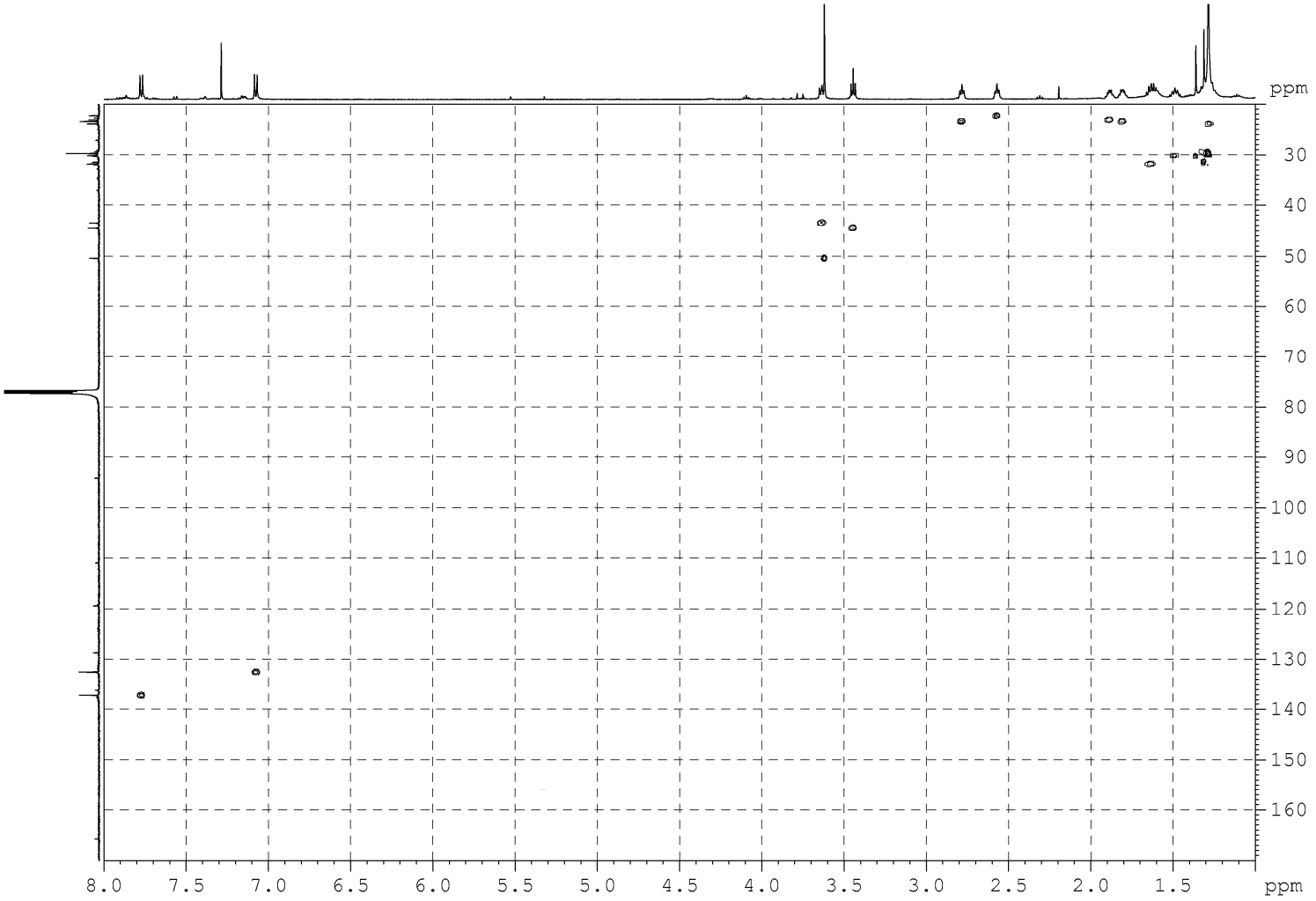

Figure S49. 2D ^{1}H-^{13}C HSQC NMR spectra of **5e** in $CDCl_3$ at T = 303 K.

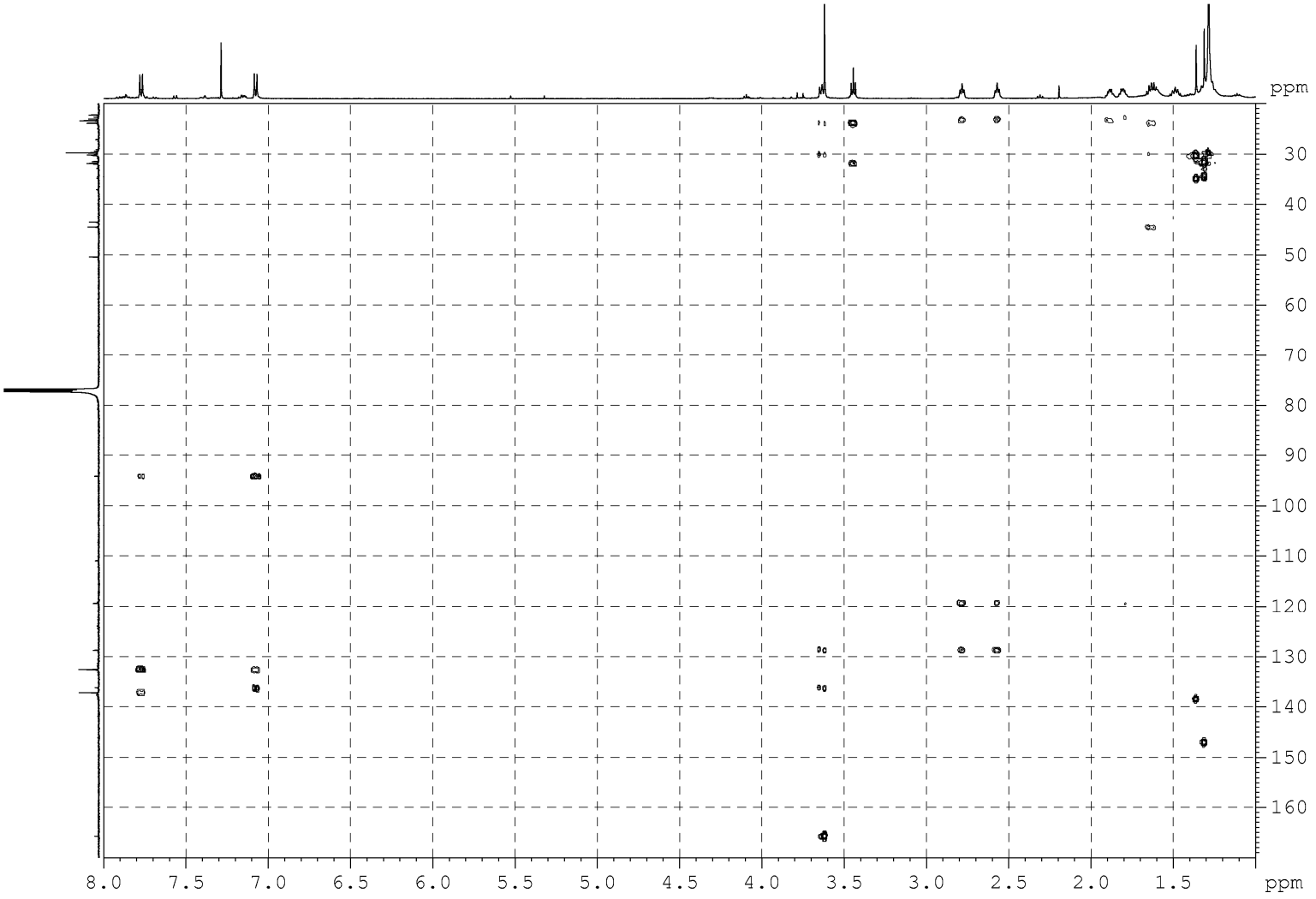

Figure S50. 2D ^{1}H-^{13}C HMBC NMR spectra of **5e** in $CDCl_3$ at T = 303 K.

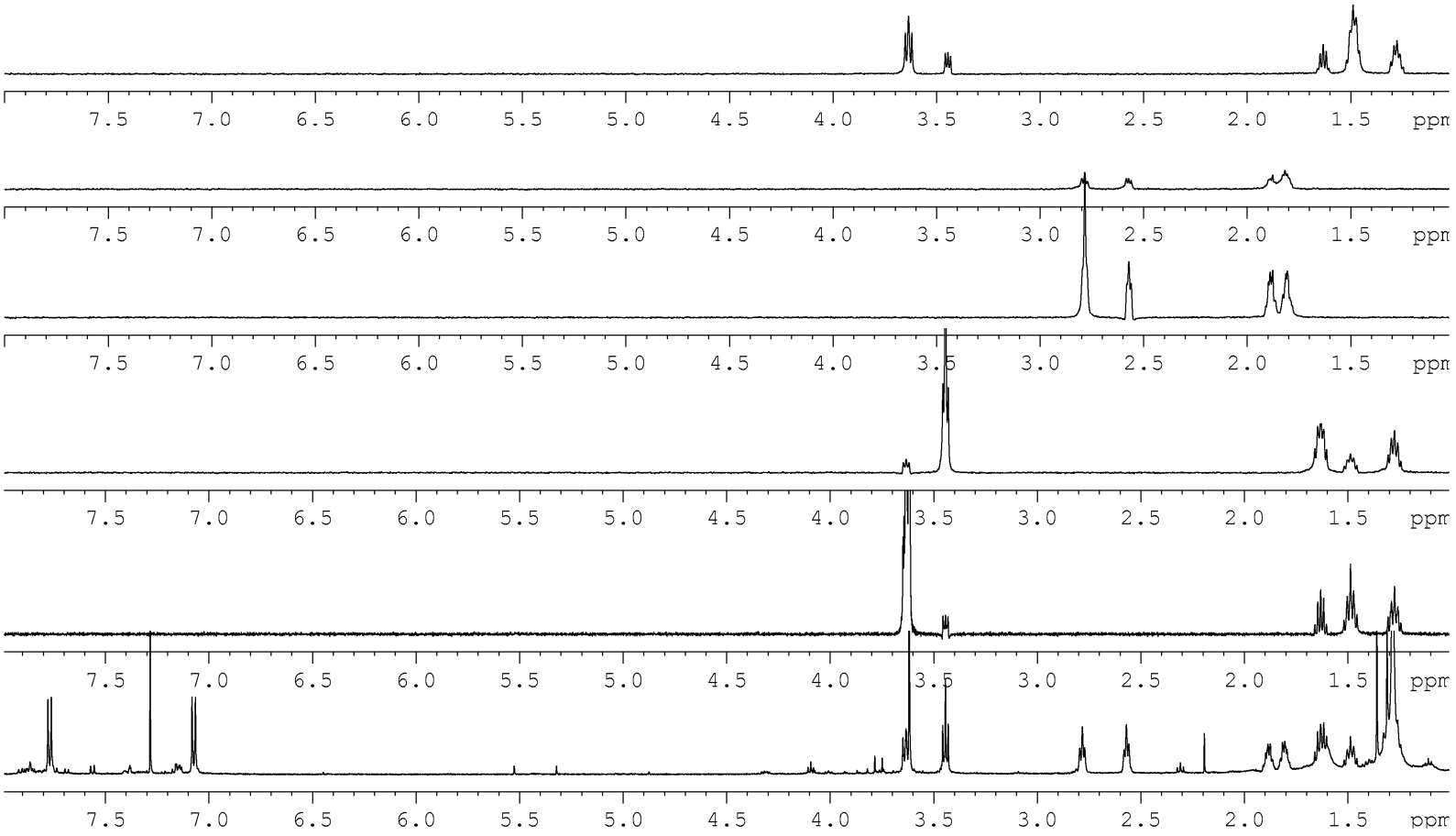

Figure S51. 1D ^{1}H and ^{1}H TOCSY NMR spectra of **5e** in $CDCl_3$ at T = 303 K.

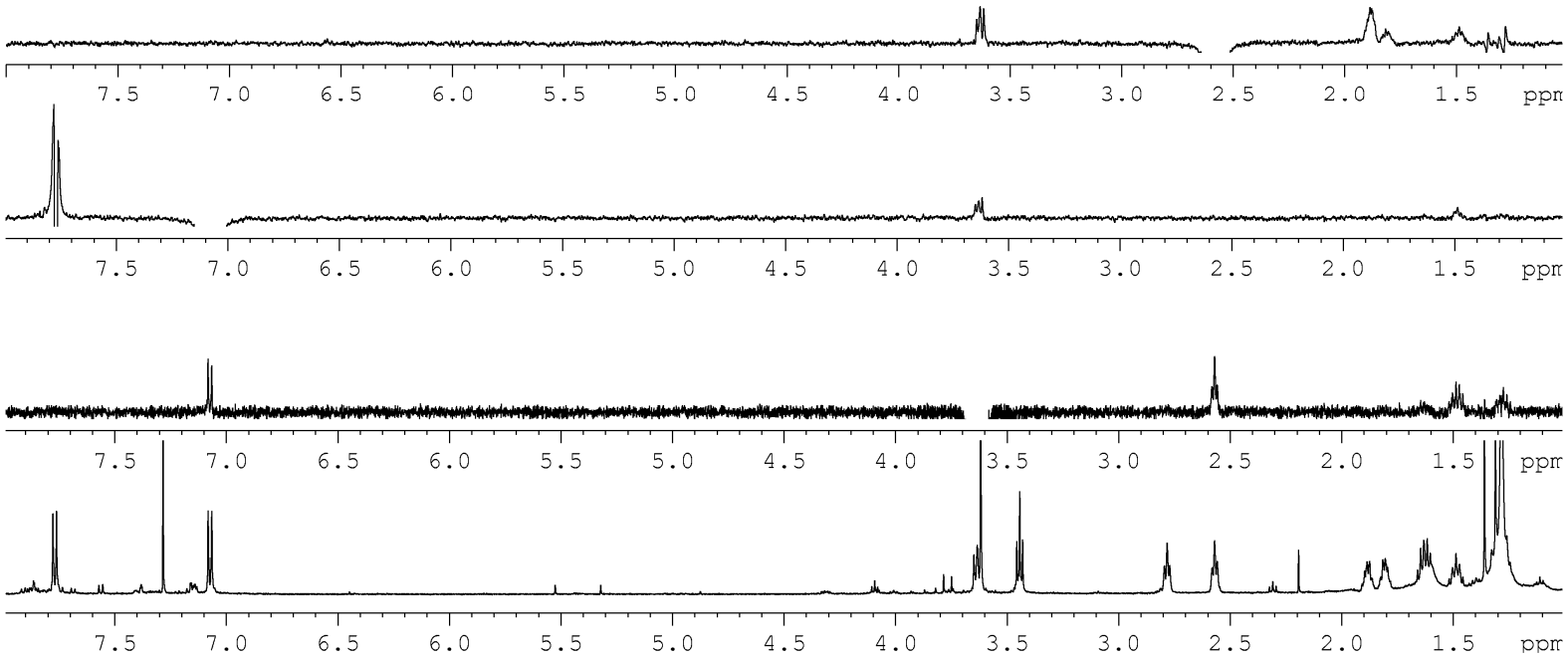

Figure S52. 1D ^{1}H and ^{1}H DPFGROE NMR spectra of **5e** in $CDCl_3$ at T = 303 K.

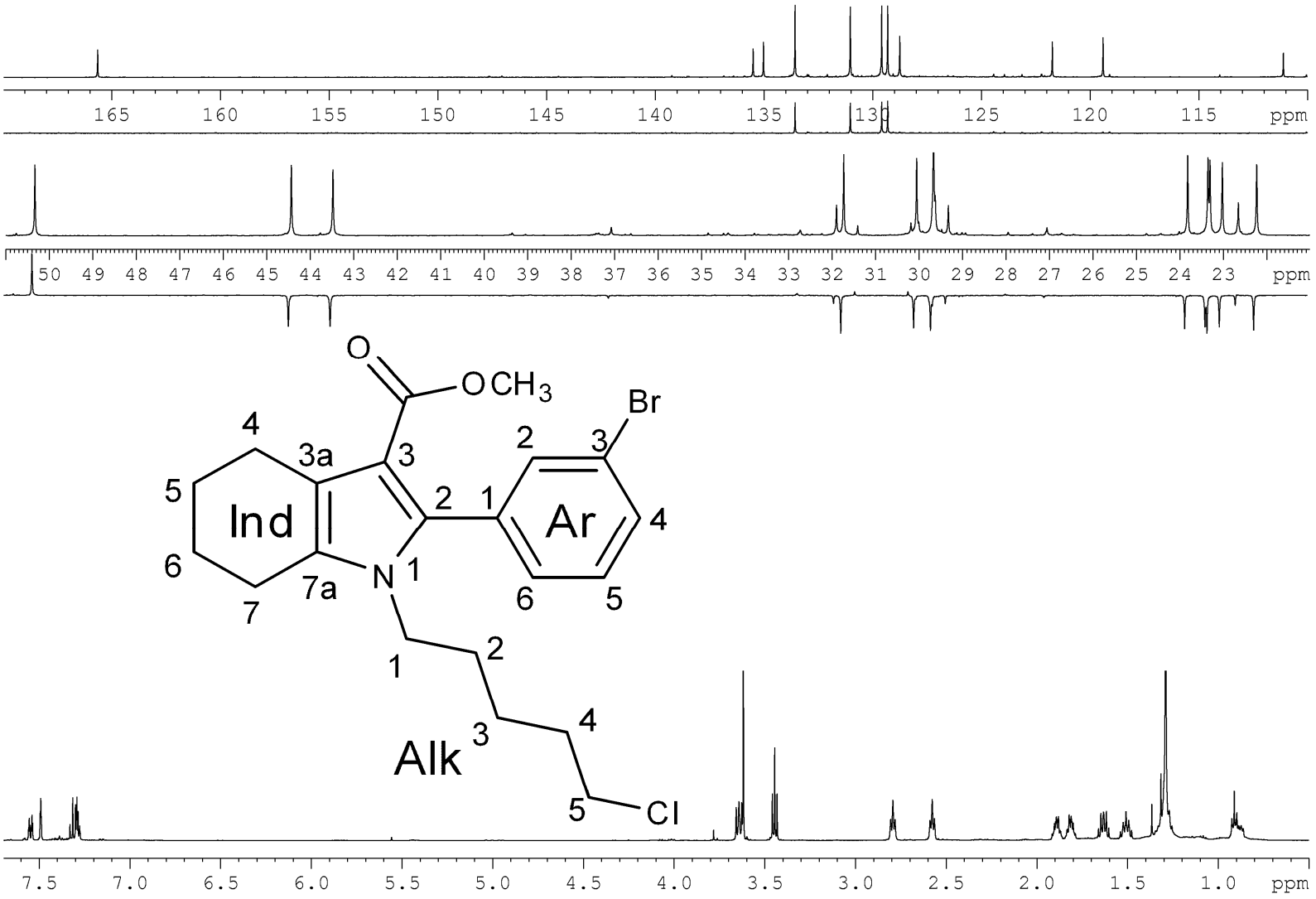

Figure S53. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **5f** in $CDCl_3$ at T = 303 K.

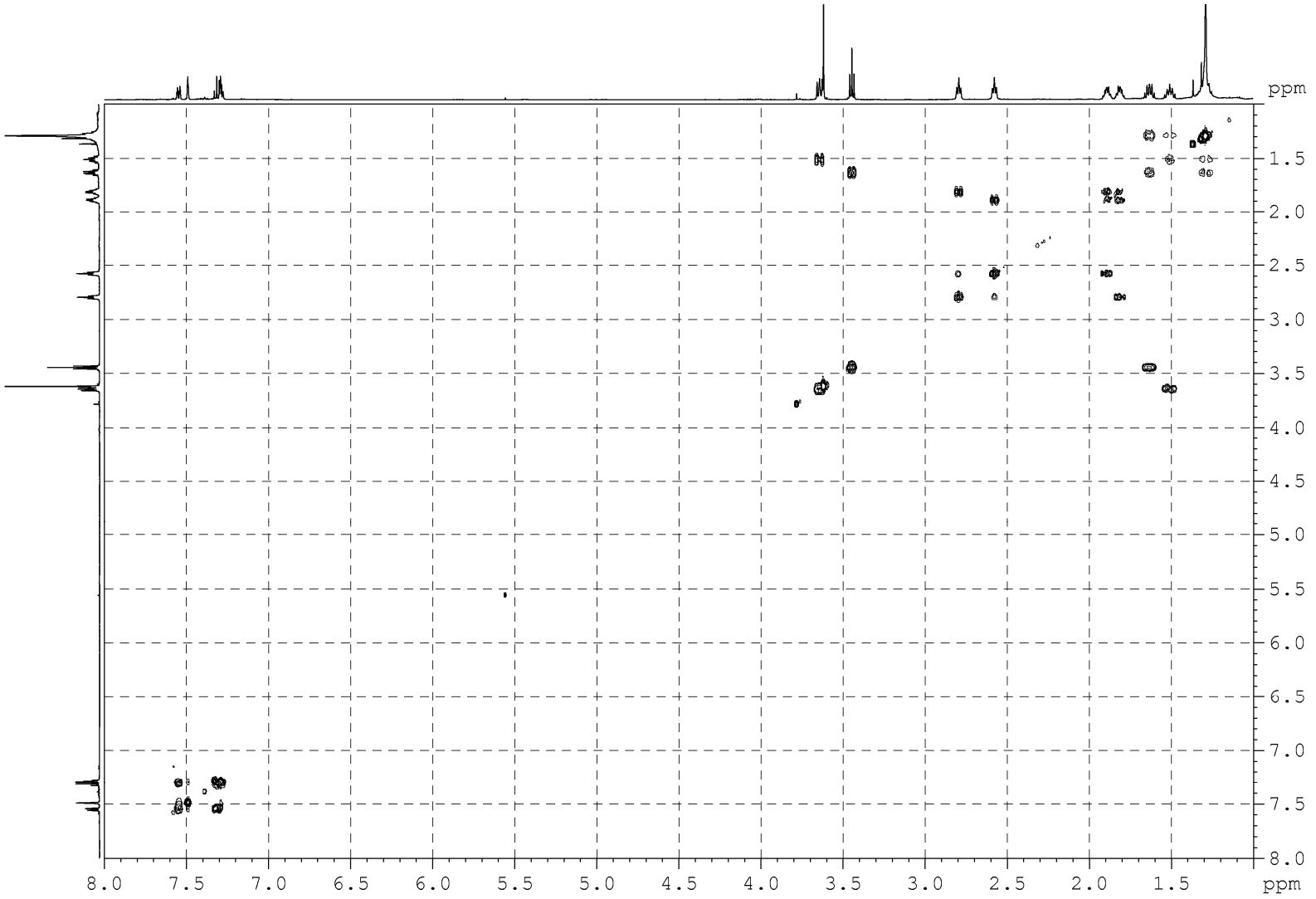

Figure S54. 2D ^{1}H-^{1}H COSY NMR spectra of **5f** in $CDCl_3$ at T = 303 K.

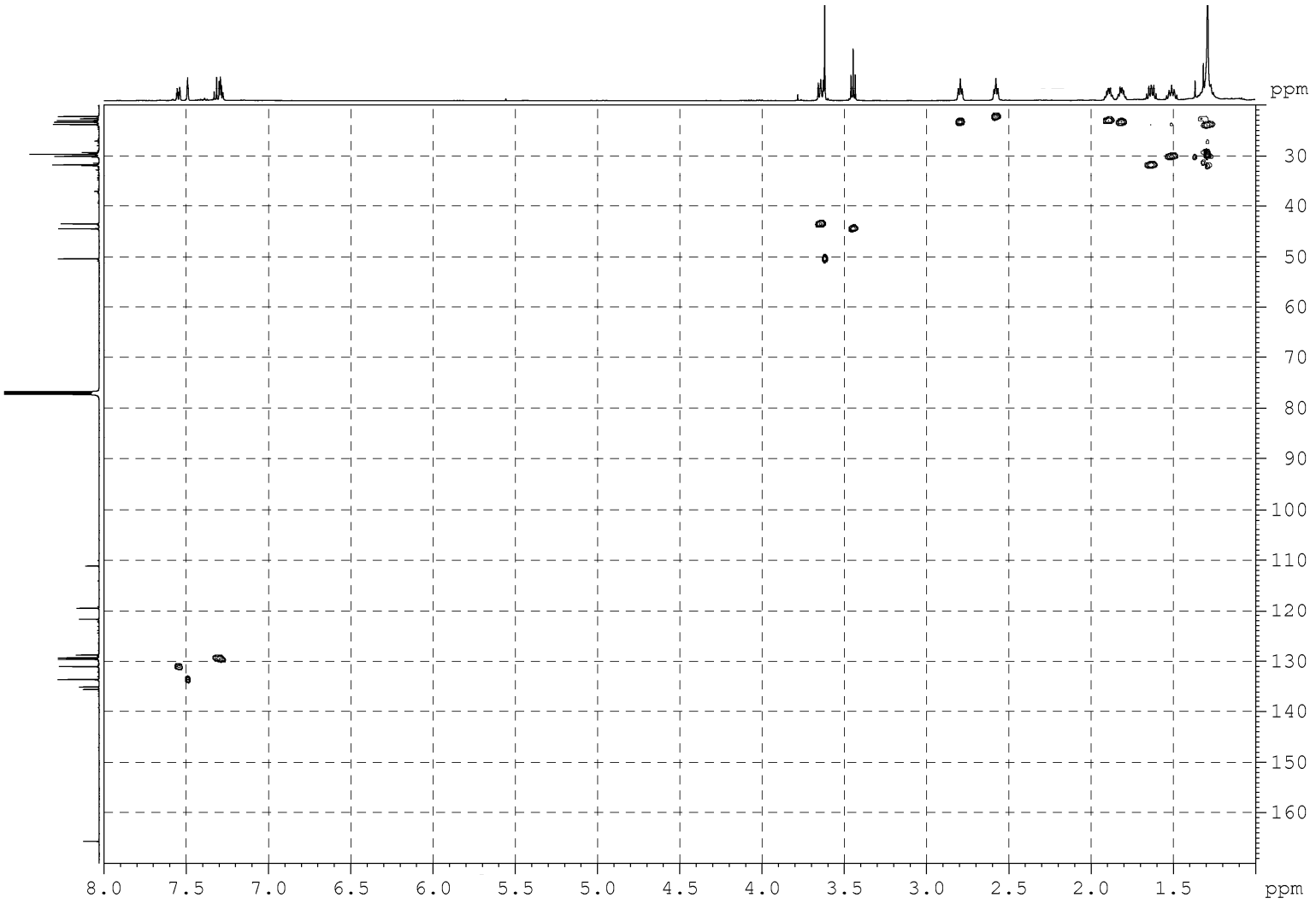

Figure S55. 2D ^{1}H-^{13}C HSQC NMR spectra of **5f** in $CDCl_3$ at T = 303 K.

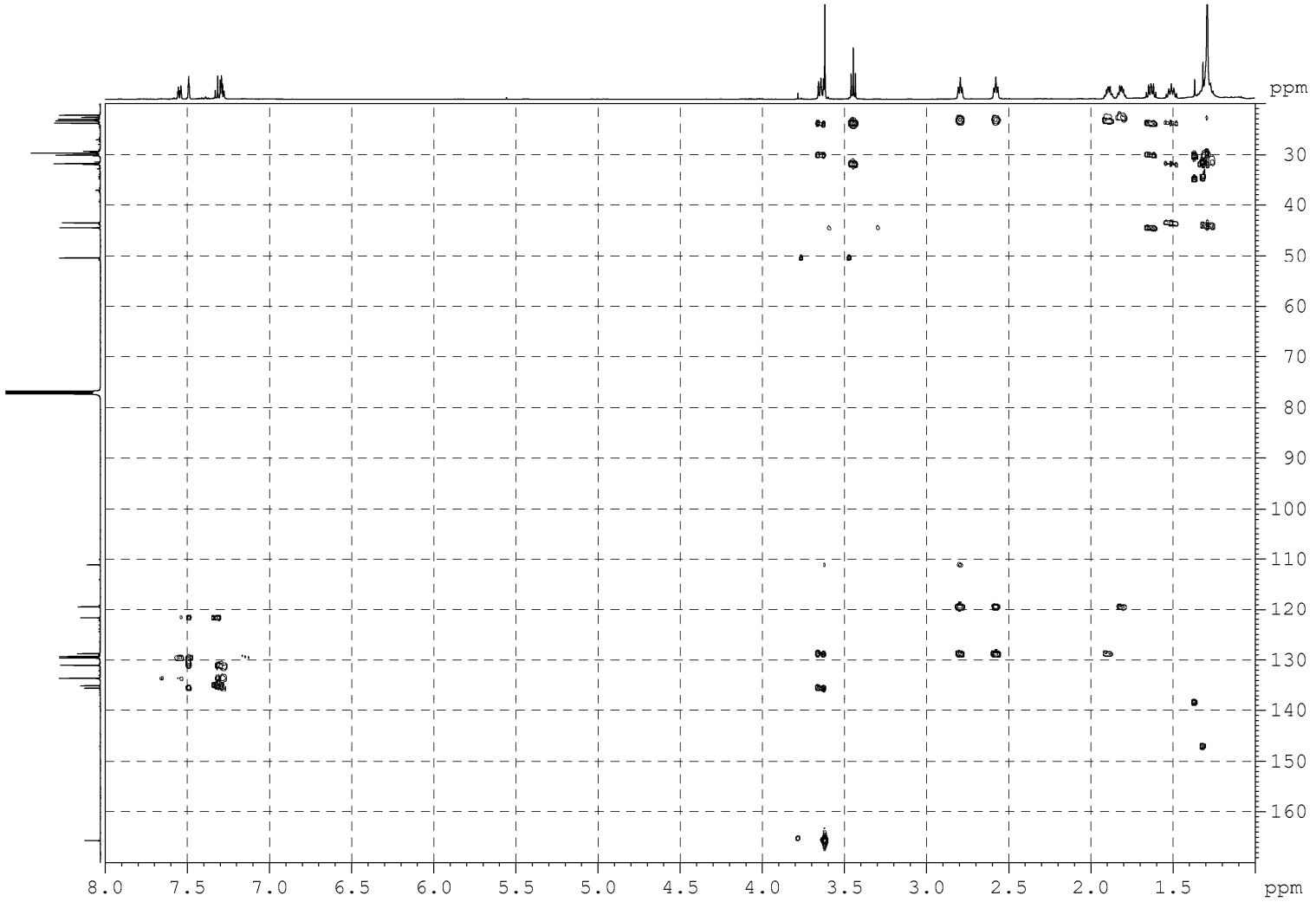

Figure S56. 2D ^{1}H-^{13}C HMBC NMR spectra of **5f** in $CDCl_3$ at T = 303 K.

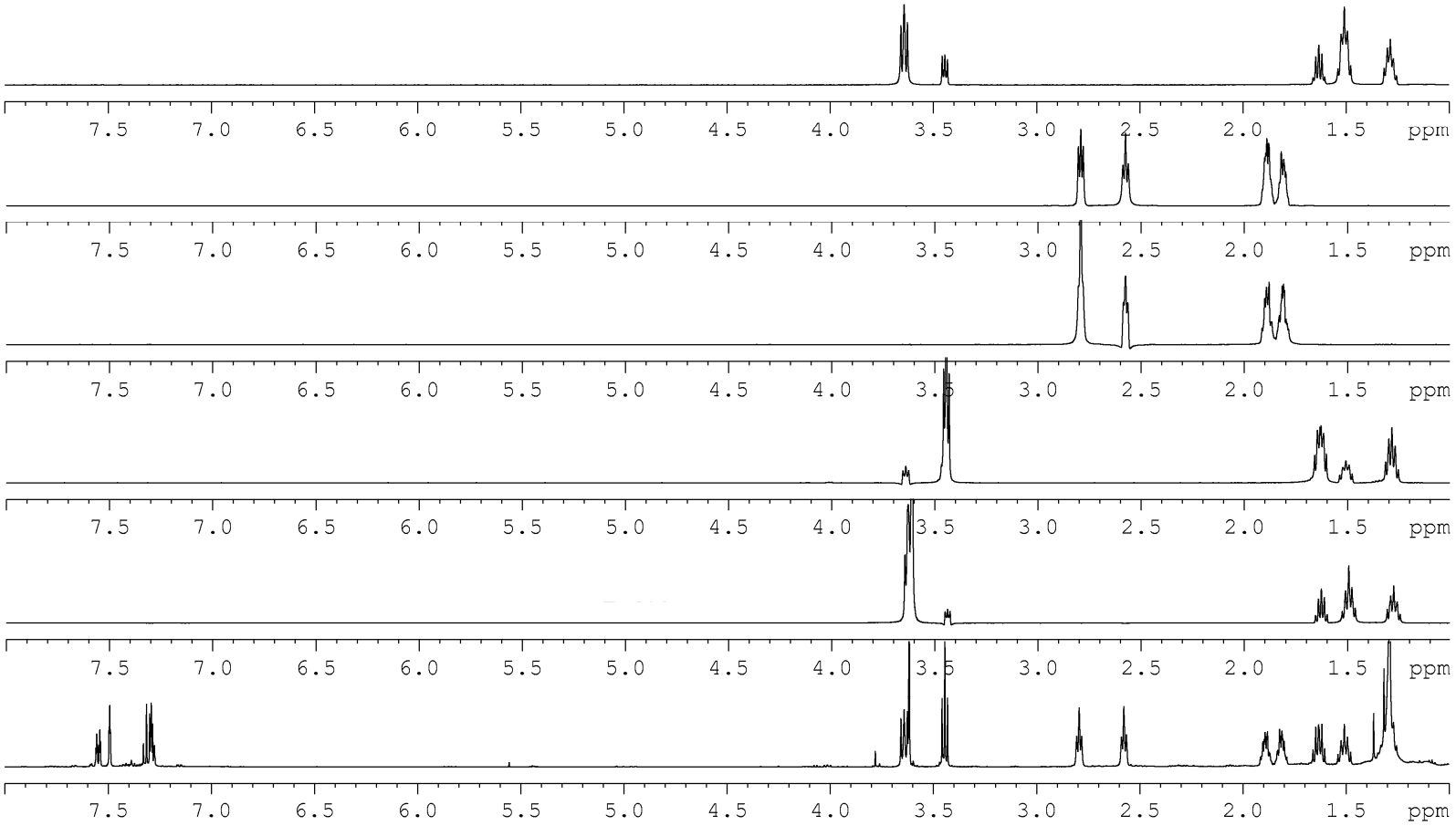

Figure S57. 1D ^{1}H and ^{1}H TOCSY NMR spectra of **5f** in $CDCl_3$ at T = 303 K.

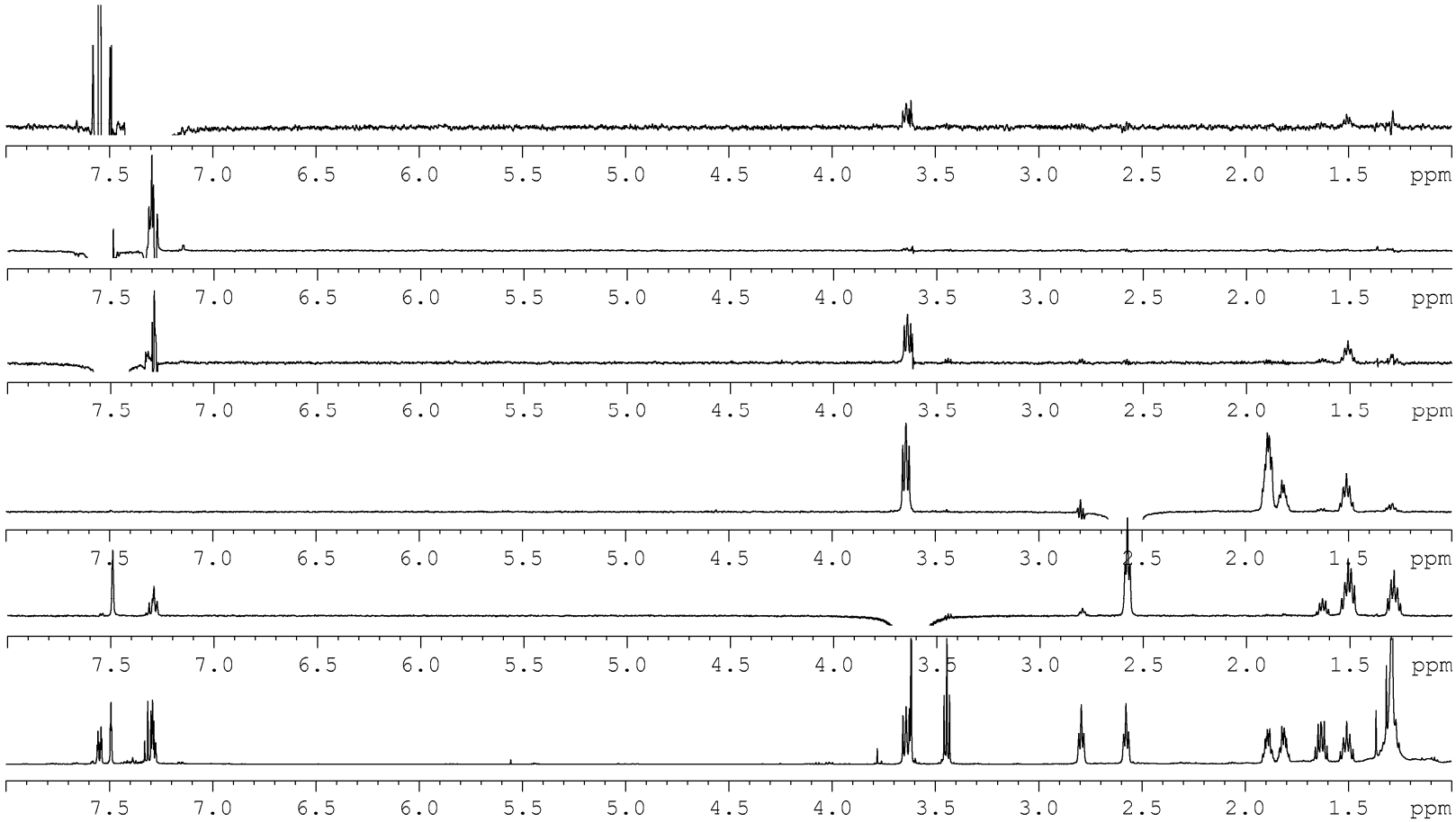

Figure S58. 1D ^{1}H and ^{1}H DPFGROE NMR spectra of **5f** in $CDCl_3$ at T = 303 K.

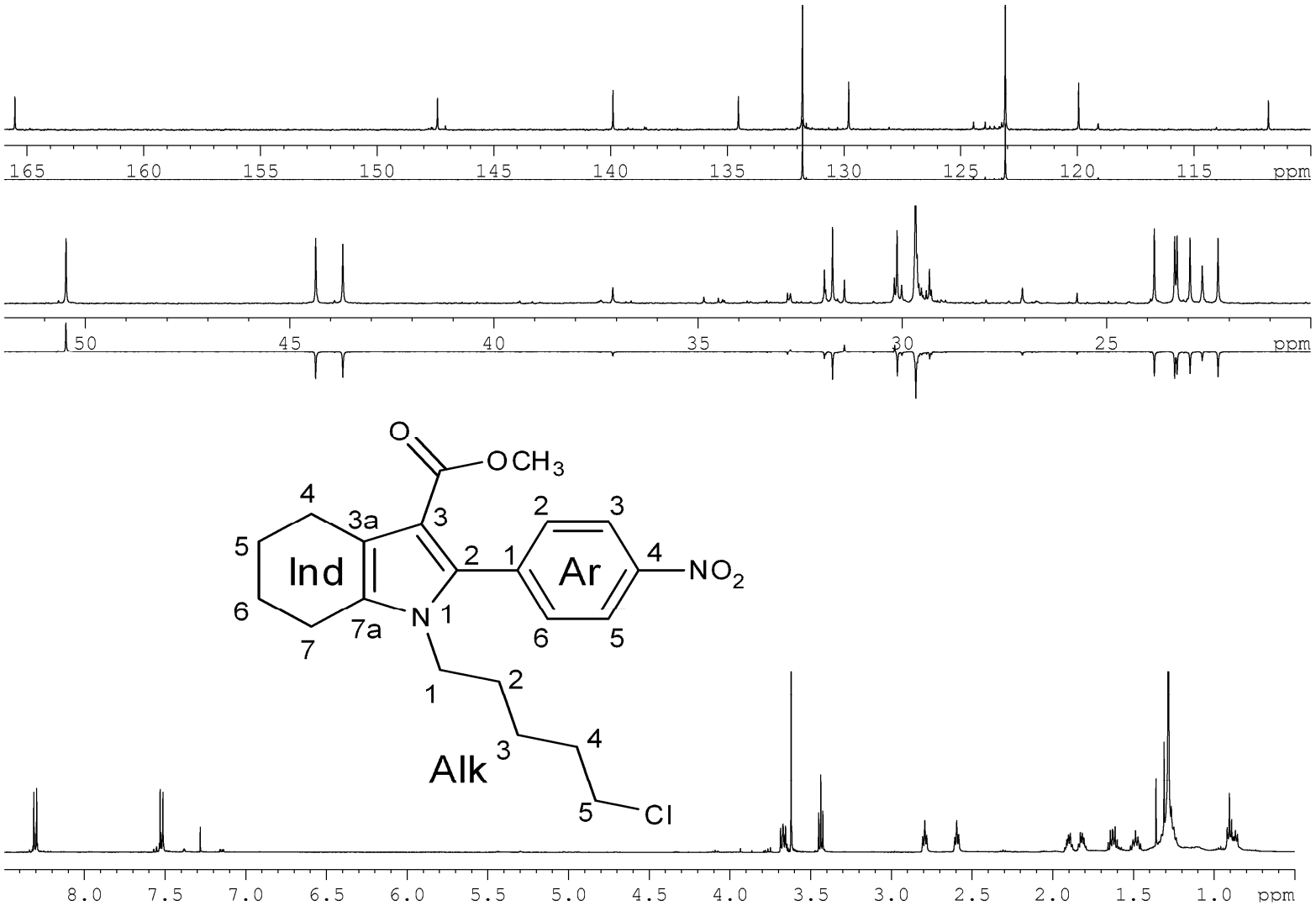

Figure S59. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **5g** in $CDCl_3$ at T = 303 K.

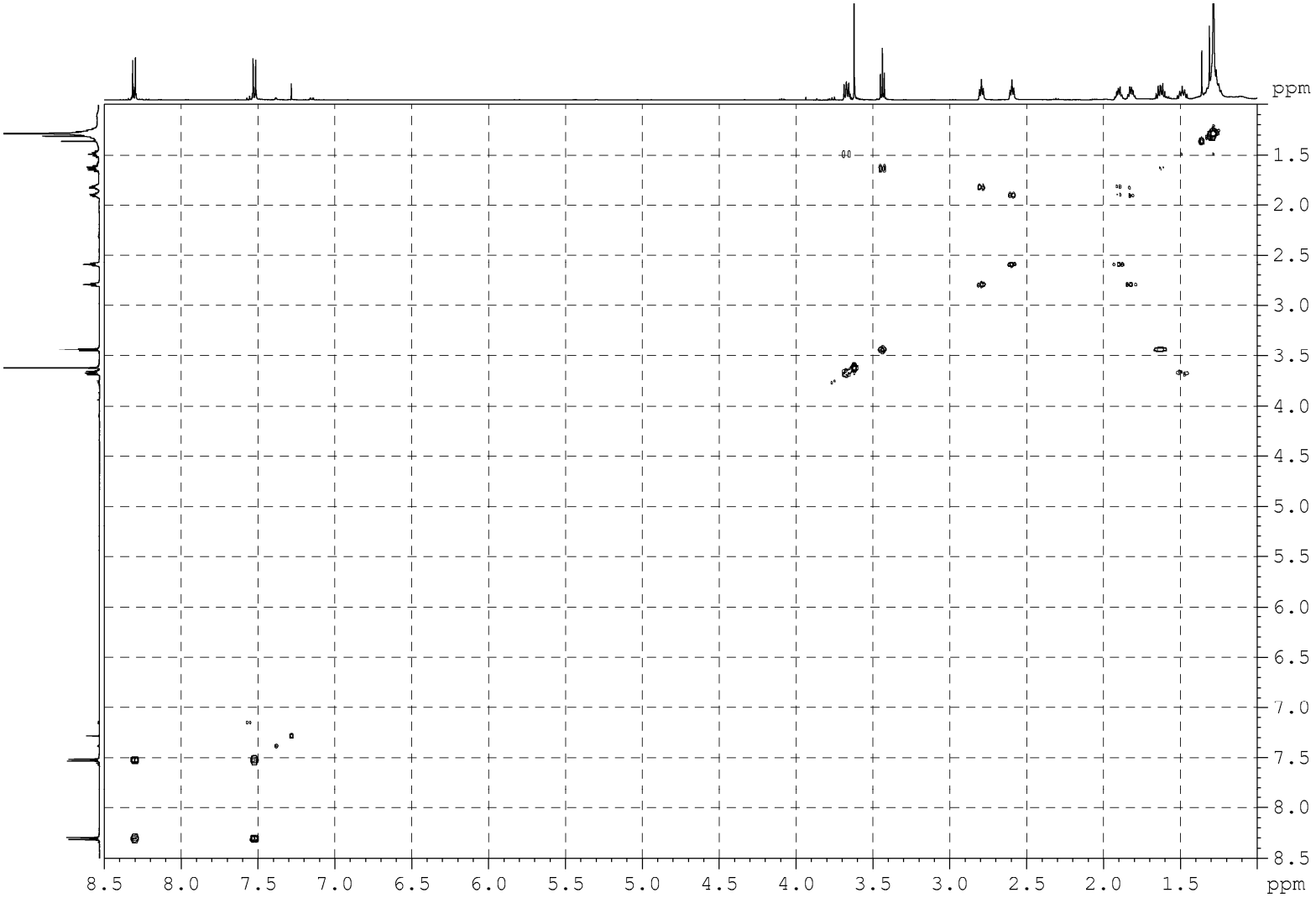

Figure S60. 2D ^{1}H-^{1}H COSY NMR spectra of **5g** in $CDCl_3$ at T = 303 K.

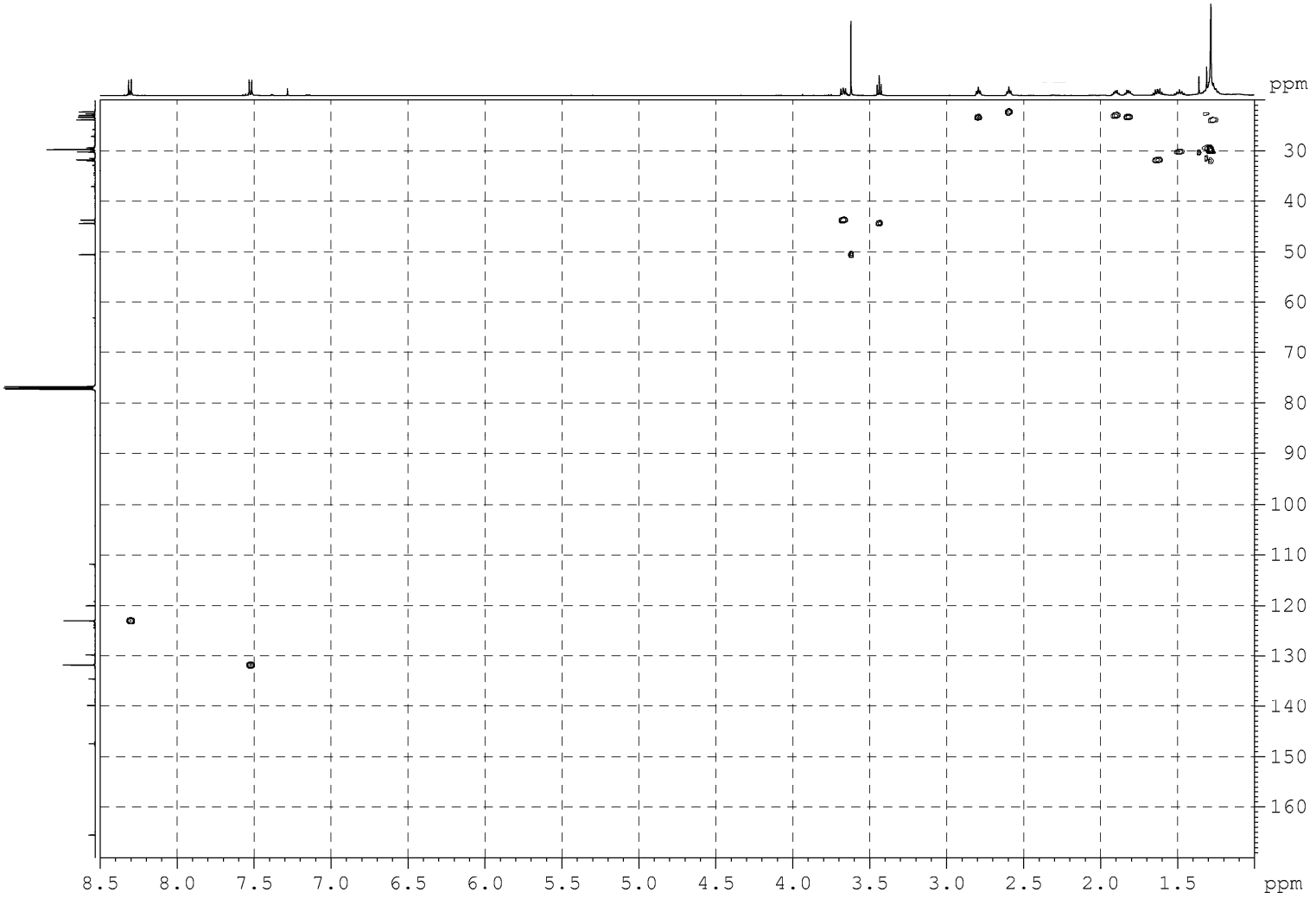

Figure S61. 2D ^{1}H-^{13}C HSQC NMR spectra of **5g** in $CDCl_3$ at T = 303 K.

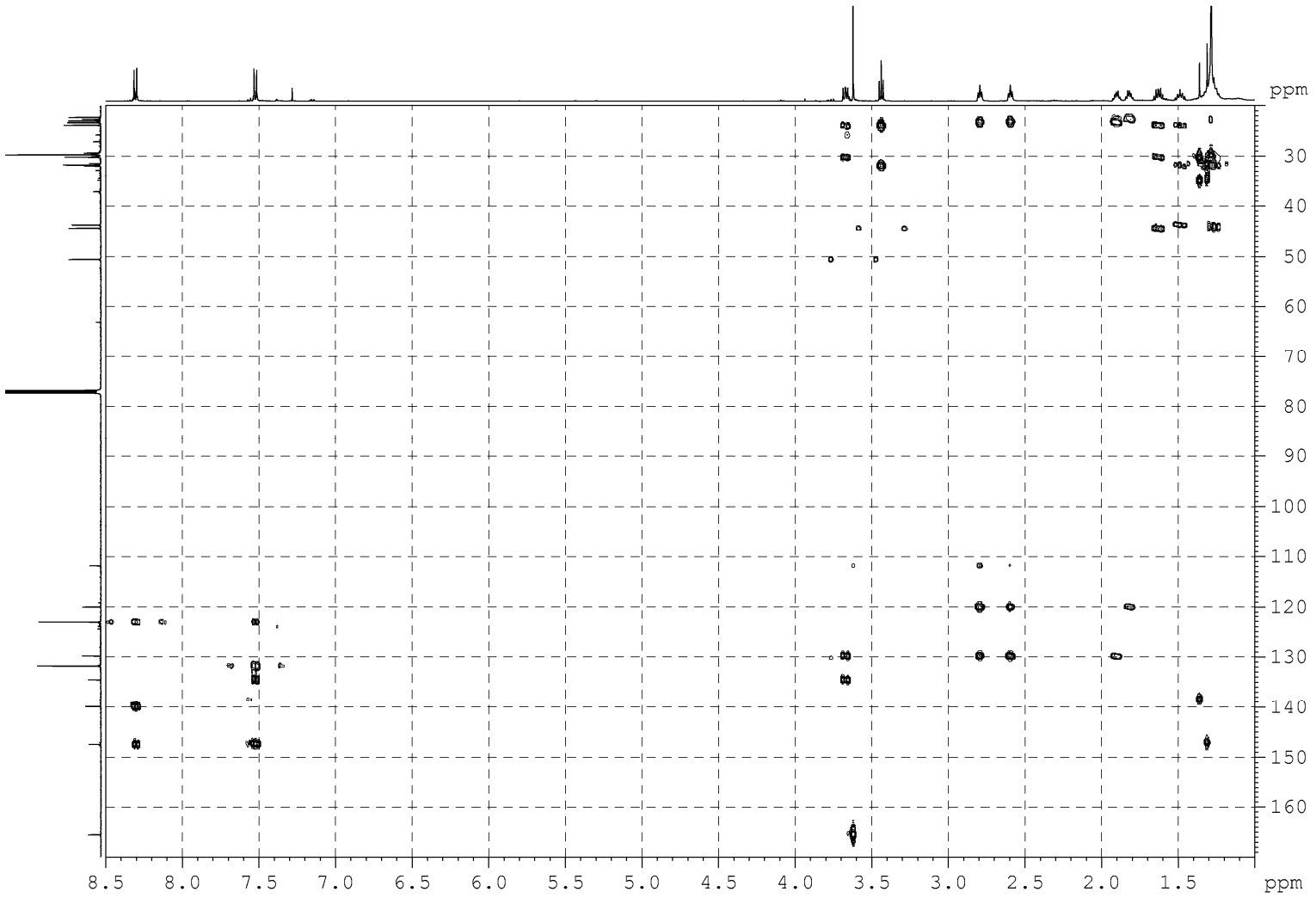

Figure S62. 2D ^{1}H-^{13}C HMBC NMR spectra of **5g** in $CDCl_3$ at T = 303 K.

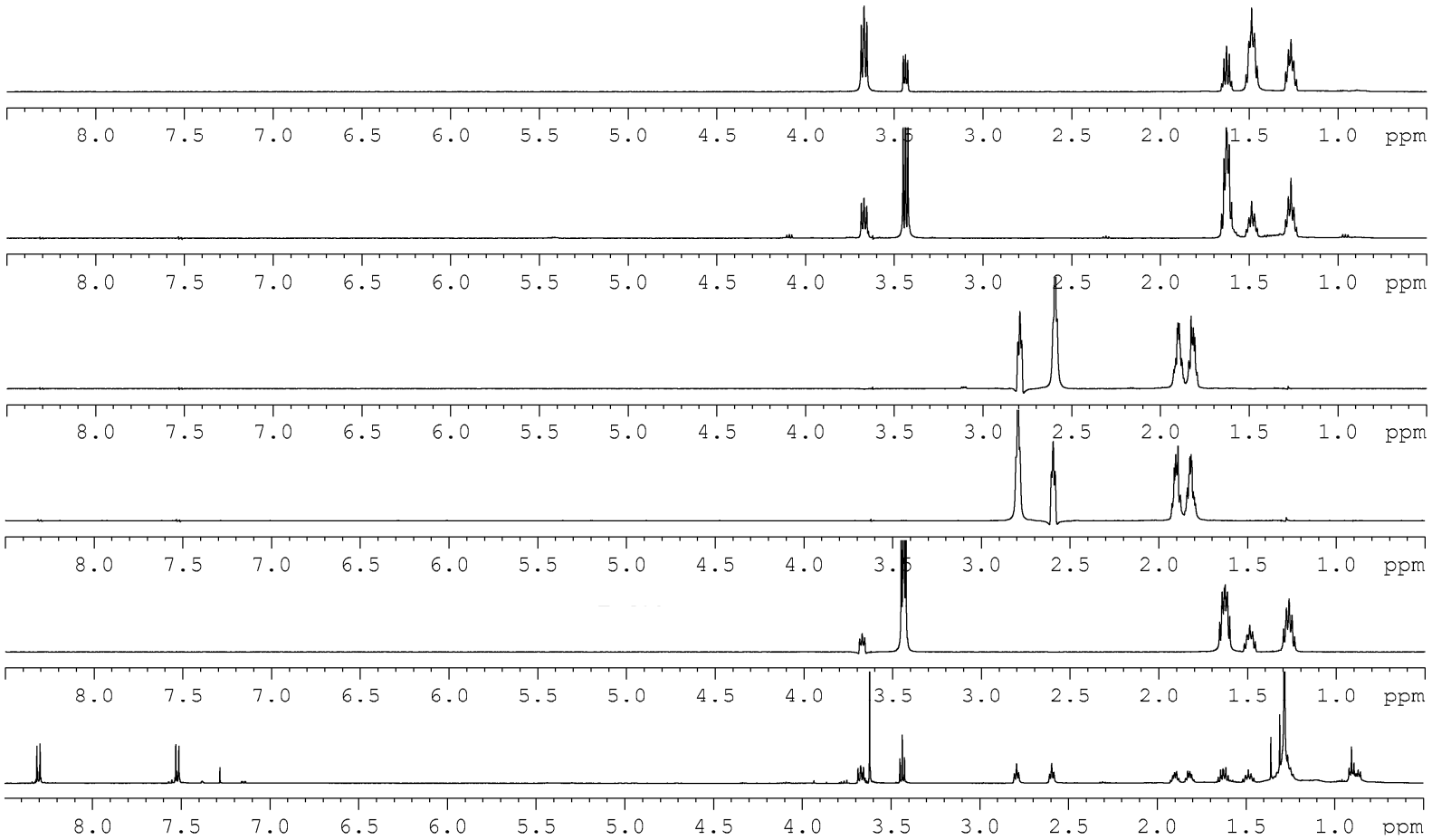

Figure S63. 1D ^{1}H and ^{1}H TOCSY NMR spectra of **5g** in $CDCl_3$ at T = 303 K.

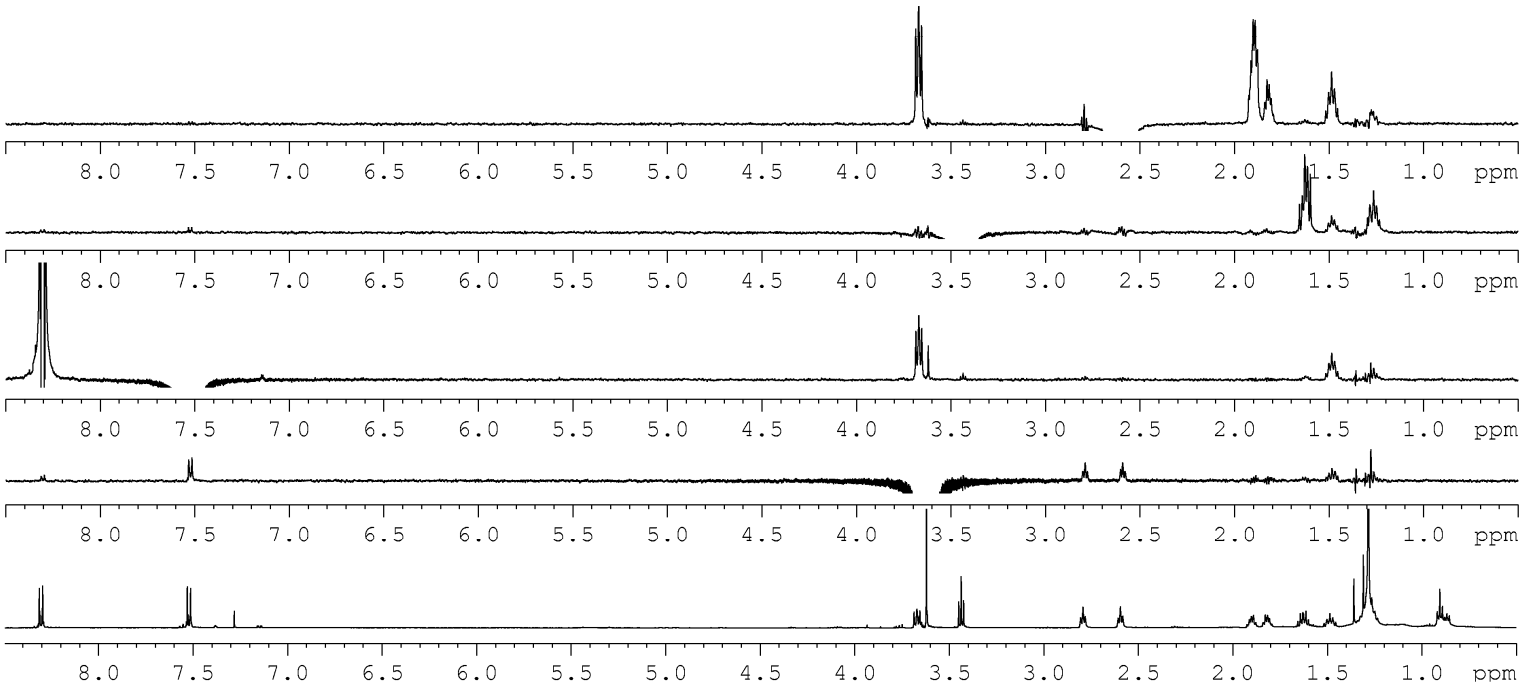

Figure S64. 1D ^{1}H and ^{1}H DPFGROE NMR spectra of **5g** in $CDCl_3$ at T = 303 K.

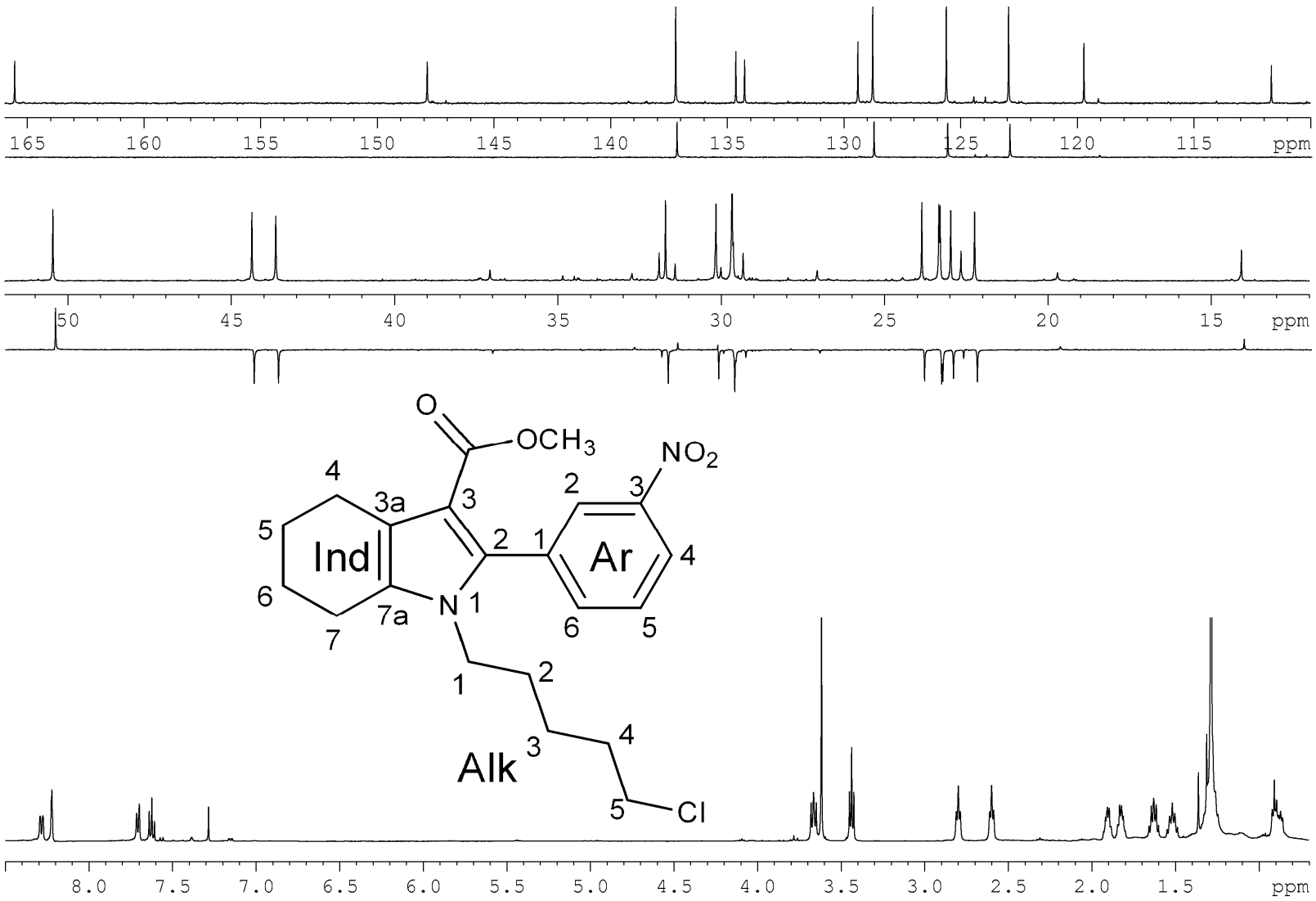

Figure S65. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **5h** in $CDCl_3$ at T = 303 K.

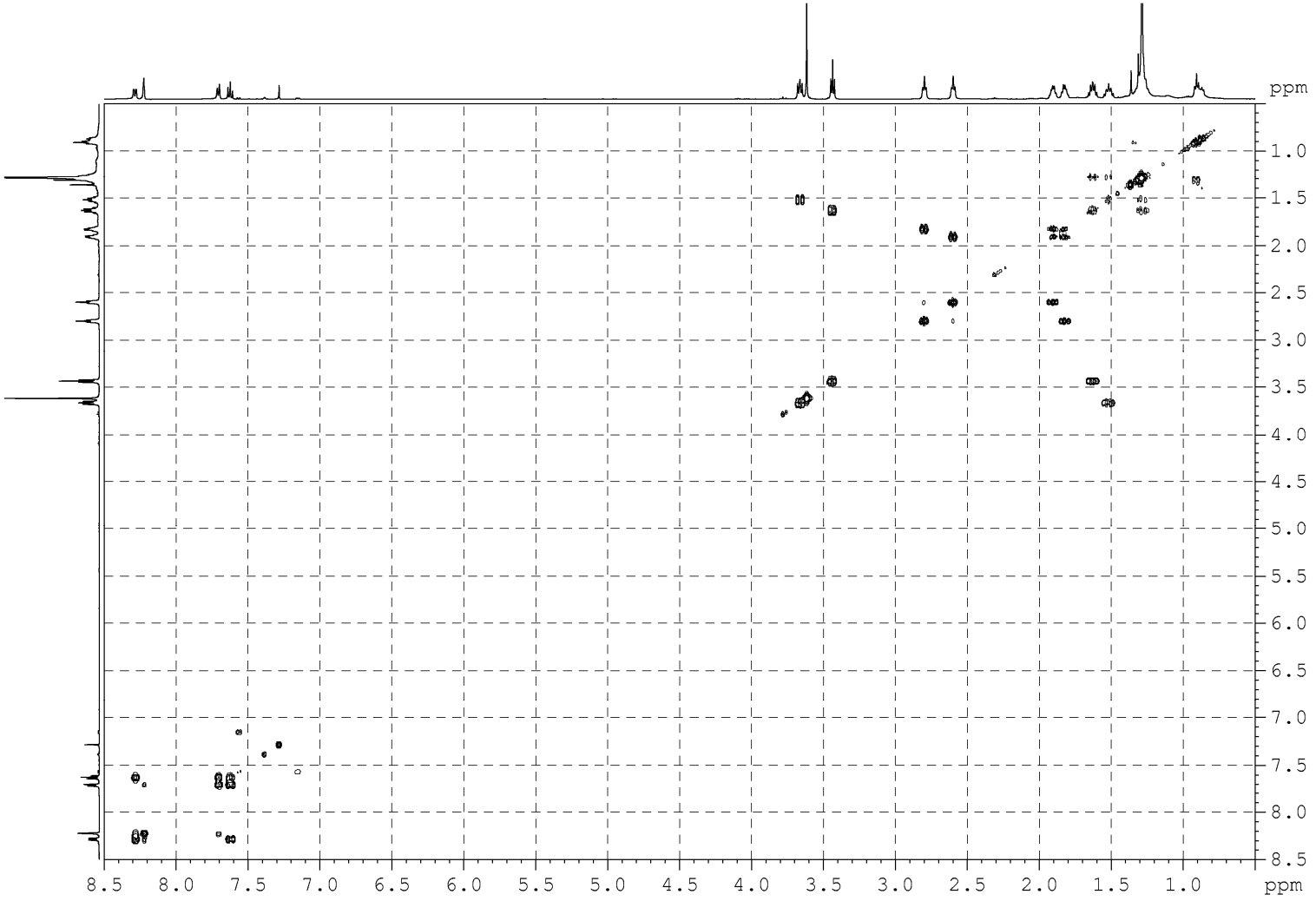

Figure S66. 2D ^{1}H-^{1}H COSY NMR spectra of **5h** in $CDCl_3$ at T = 303 K.

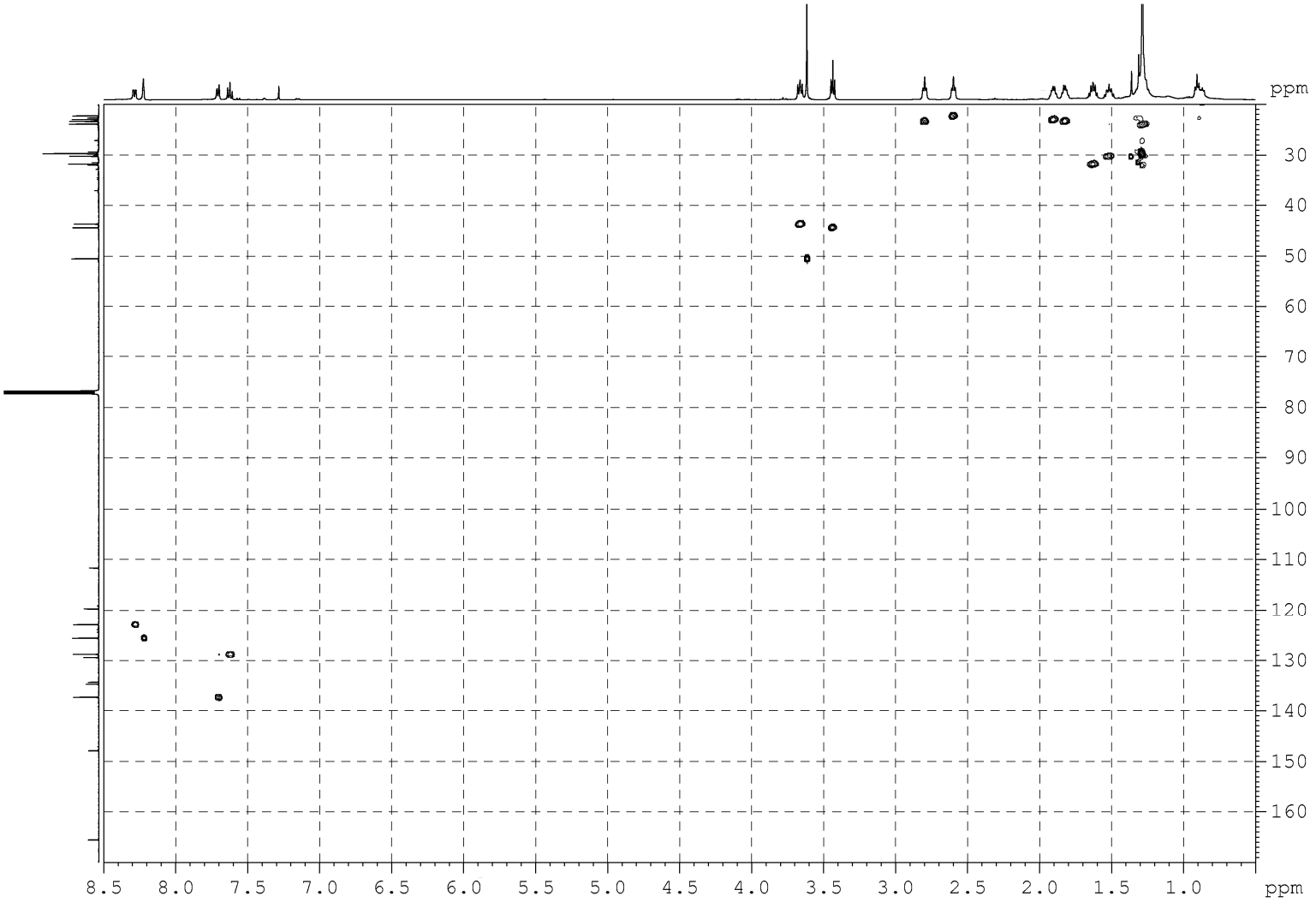

Figure S67. 2D ^{1}H-^{13}C HSQC NMR spectra of **5h** in $CDCl_3$ at T = 303 K.

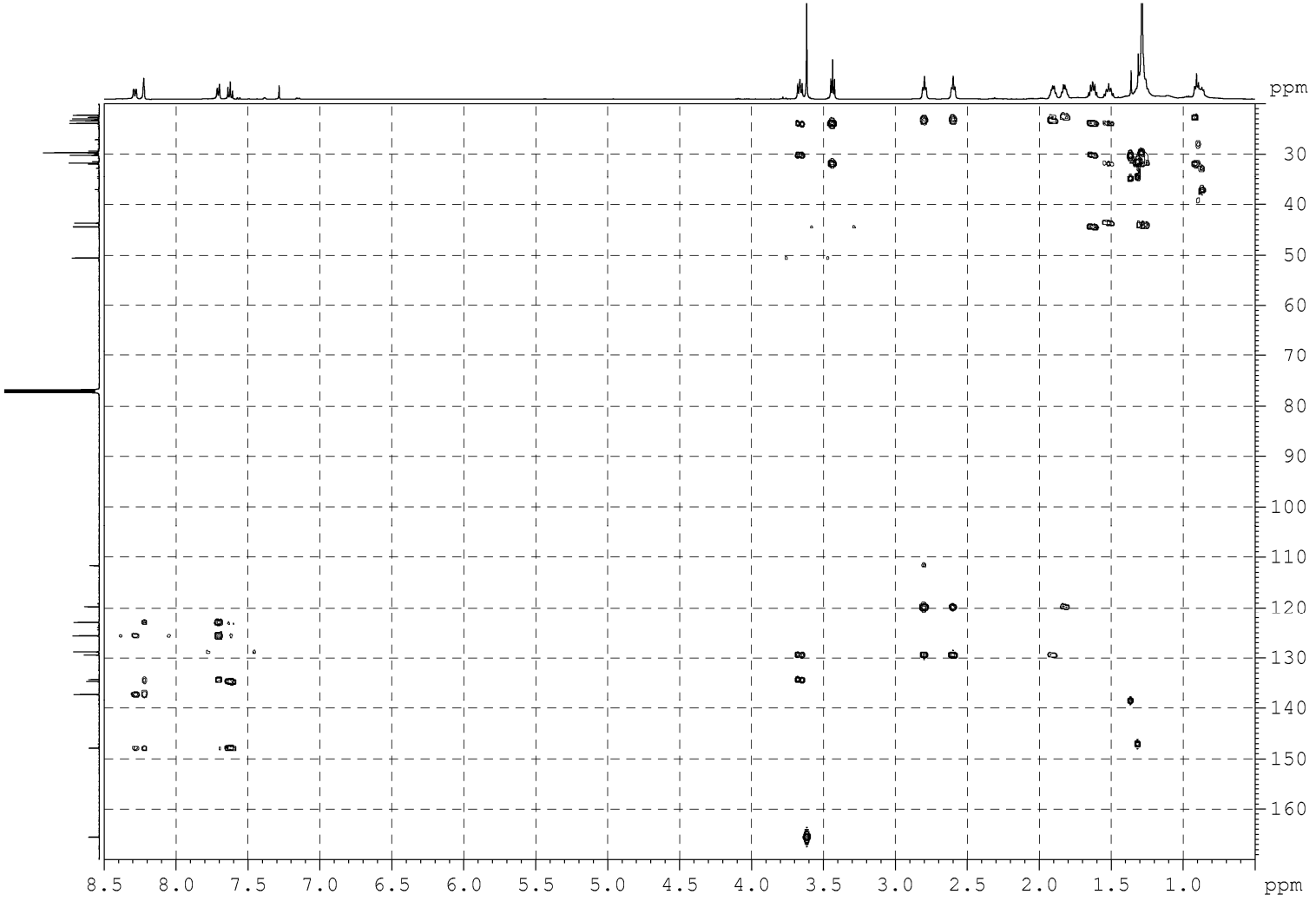

Figure S68. 2D ^{1}H-^{13}C HMBC NMR spectra of **5h** in $CDCl_3$ at T = 303 K.

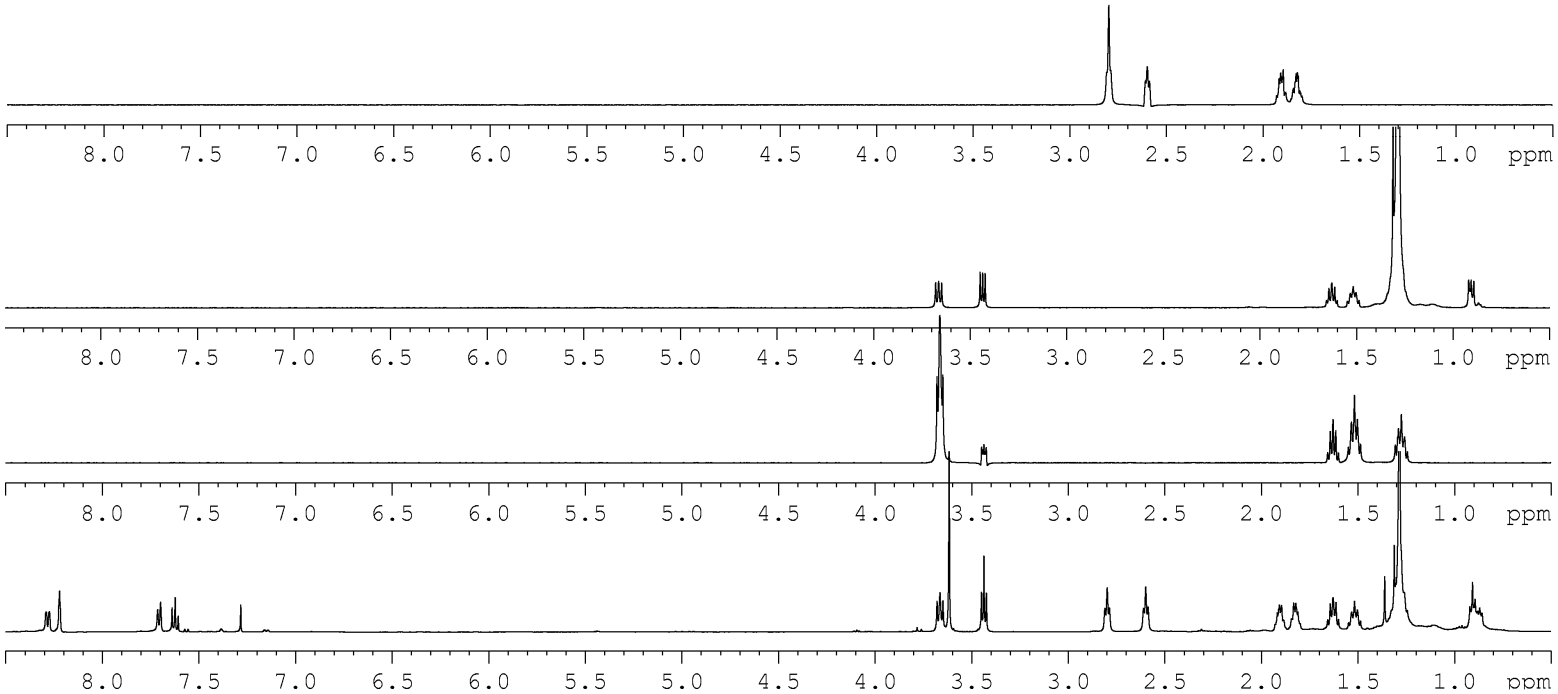

Figure S69. 1D ^{1}H and ^{1}H TOCSY NMR spectra of **5d** in $CDCl_3$ at T = 303 K.

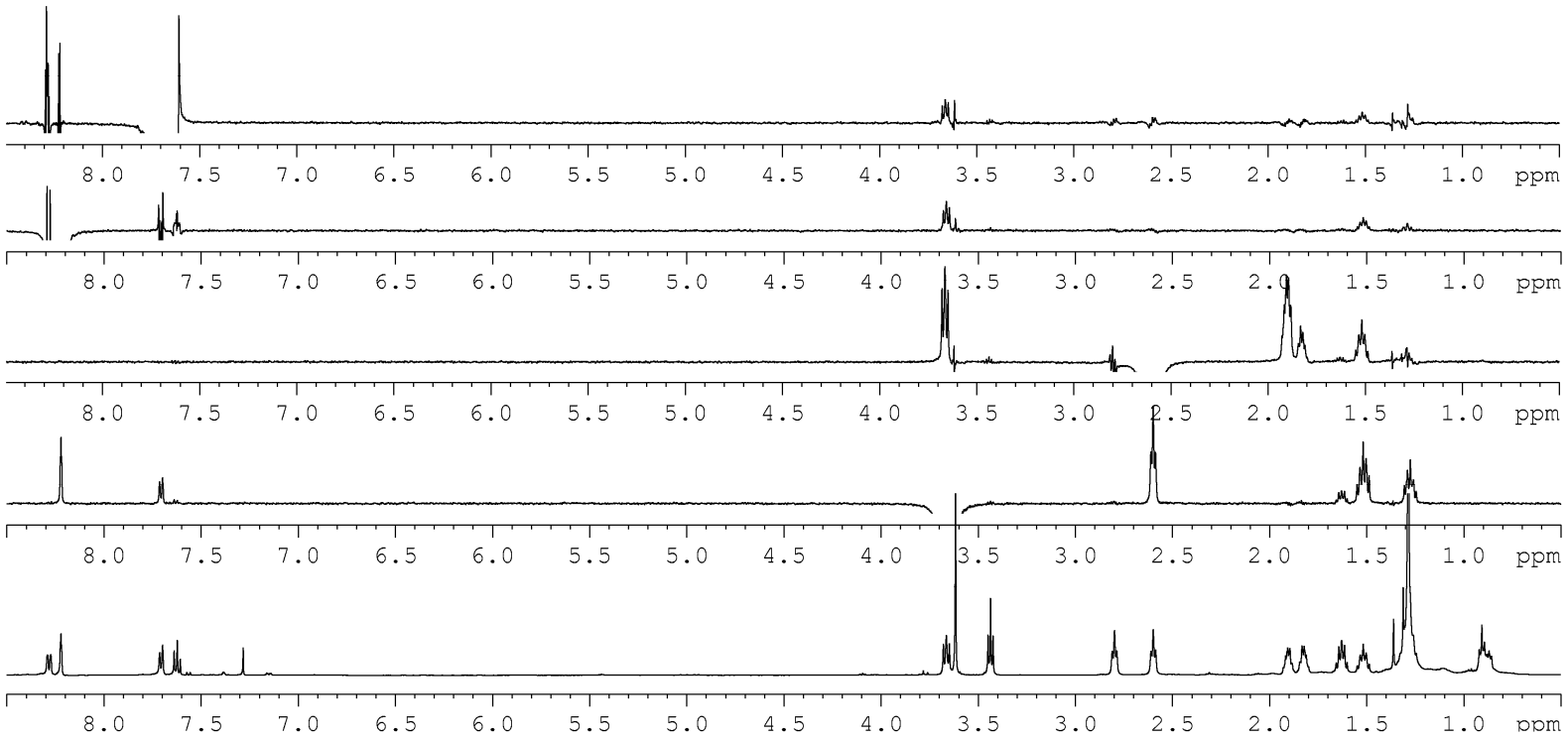

Figure S70. 1D ^{1}H and ^{1}H DPFGROE NMR spectra of **5h** in $CDCl_3$ at T = 303 K.

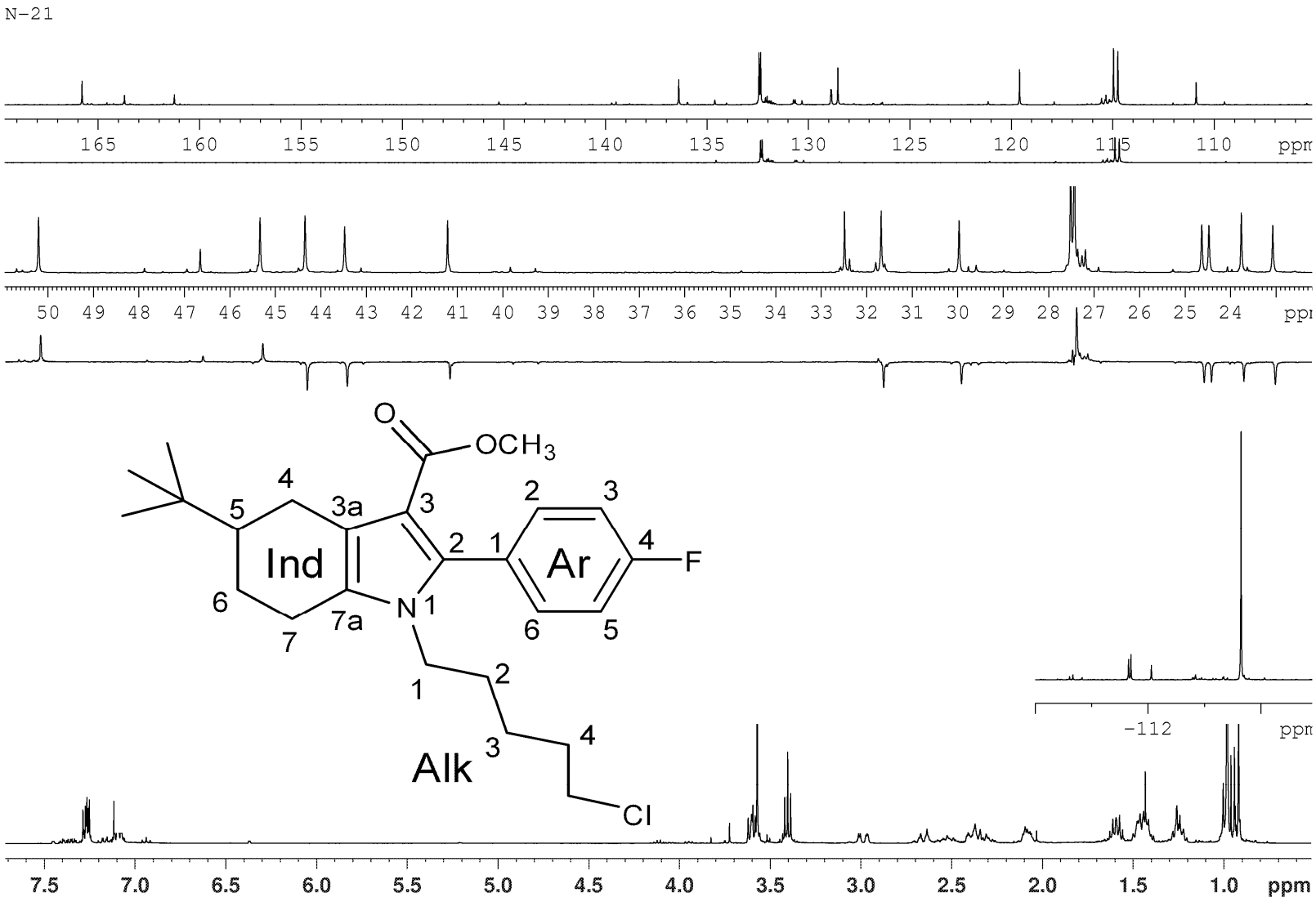

Figure S71. 1D ^{1}H, ^{13}C DEPT, $^{13}C\{^{1}H\}$ and $^{19}F\{^{1}H\}$ NMR spectra of **5i** in $CDCl_3$ at T = 303 K.

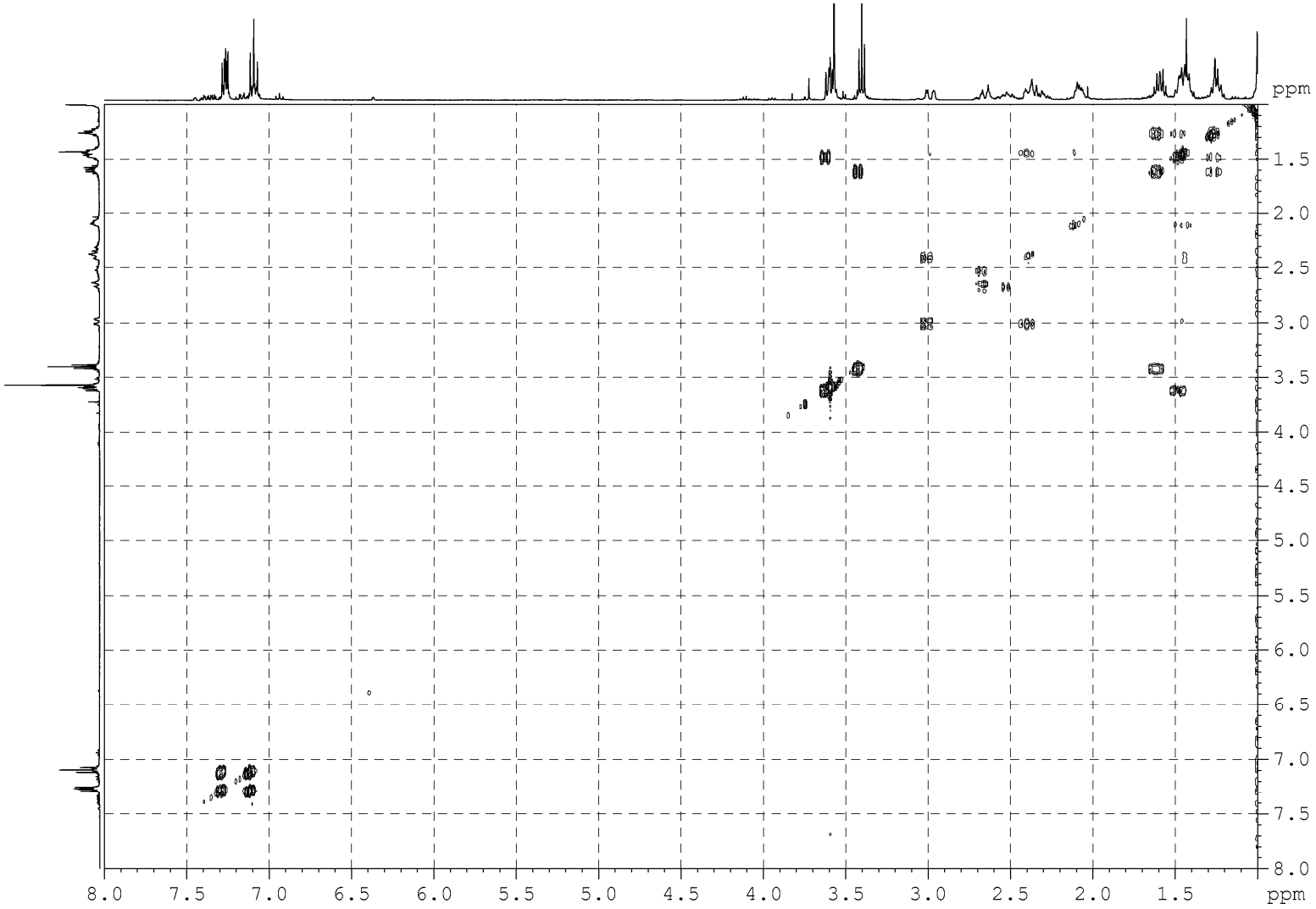

Figure S72. 2D ^{1}H-^{1}H COSY NMR spectra of **5i** in $CDCl_3$ at T = 303 K.

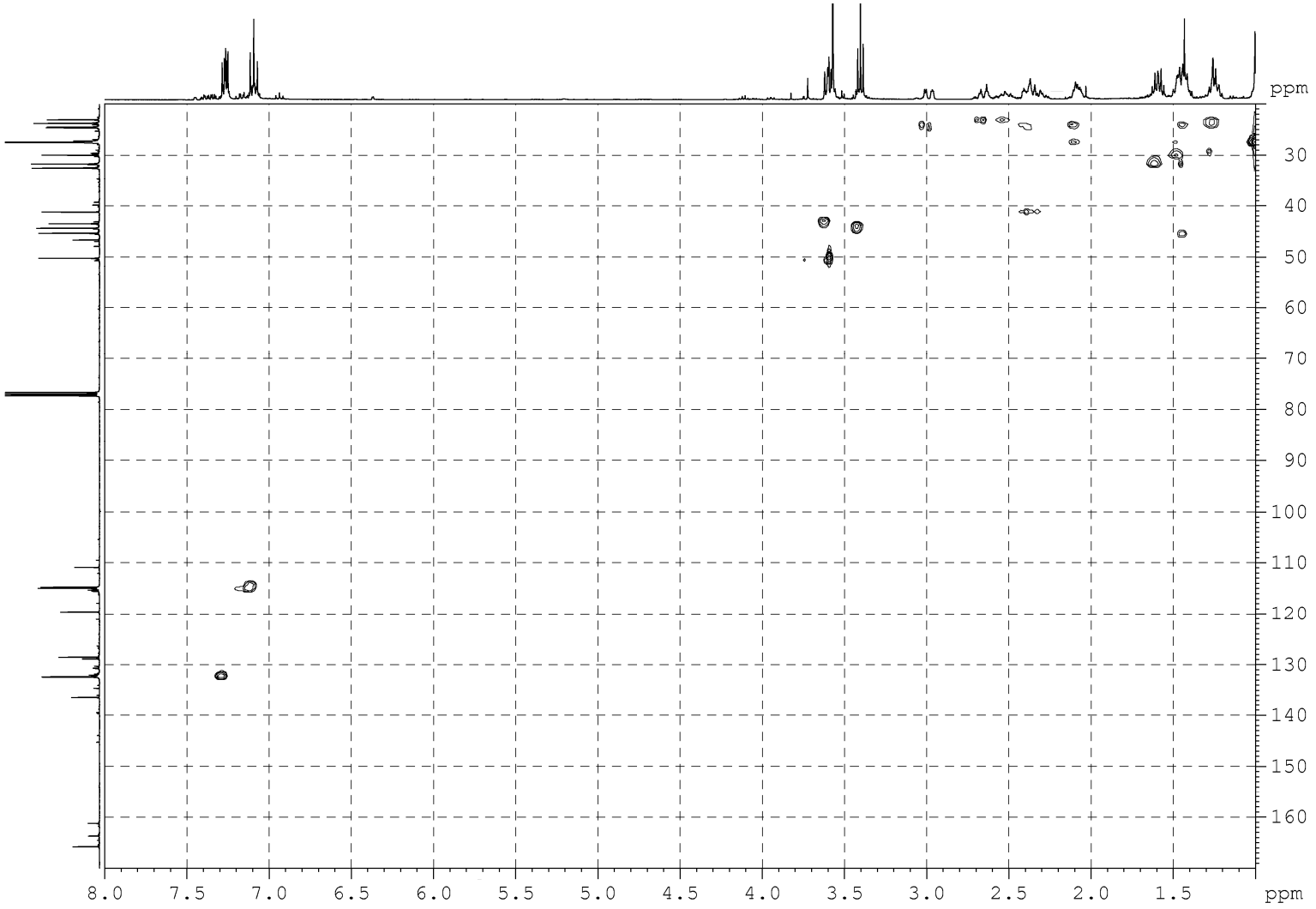

Figure S73. 2D ^{1}H-^{13}C HSQC NMR spectra of **5i** in $CDCl_3$ at T = 303 K.

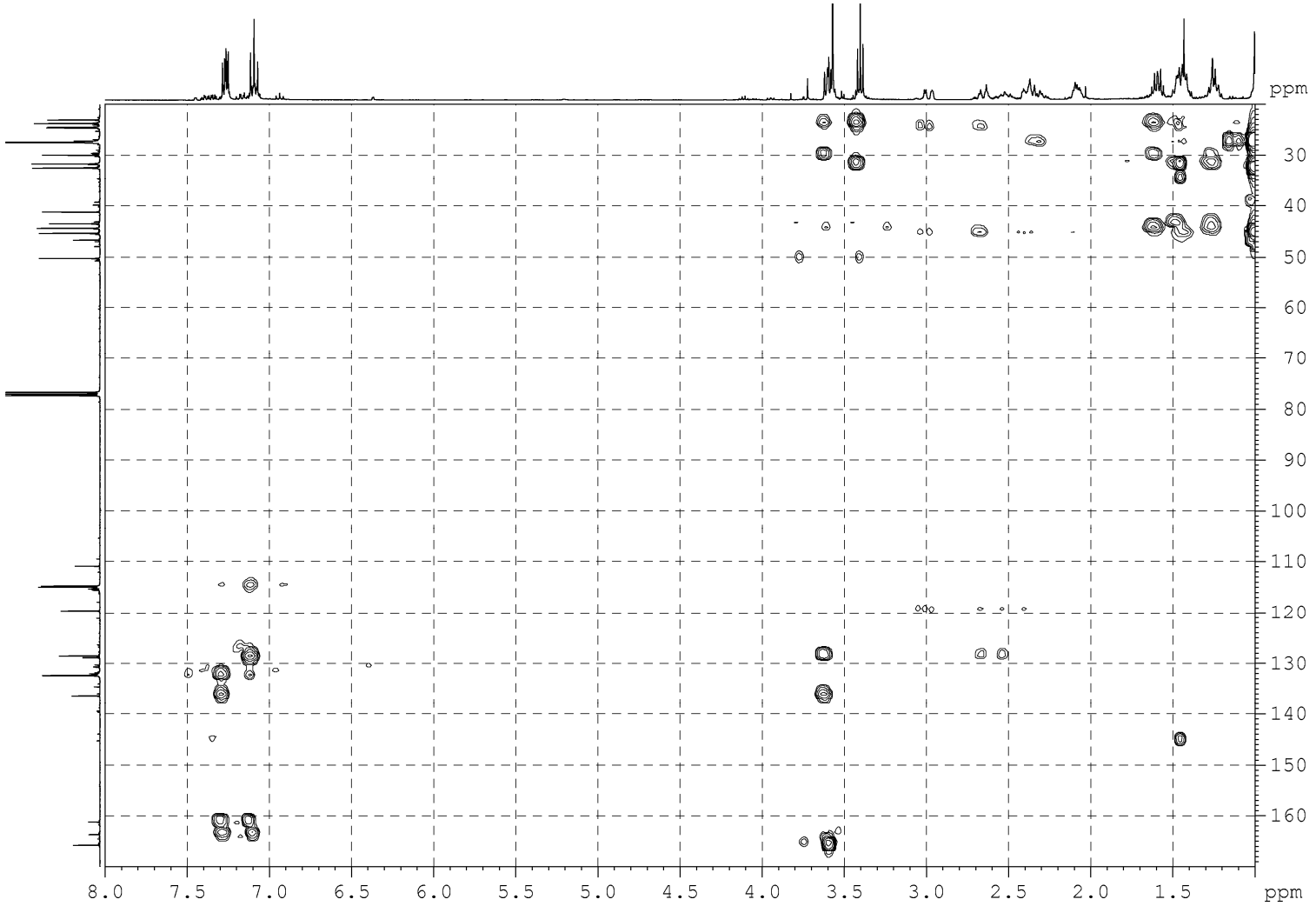

Figure S74. 2D ^{1}H-^{13}C HMBC NMR spectra of **5i** in $CDCl_3$ at T = 303 K.

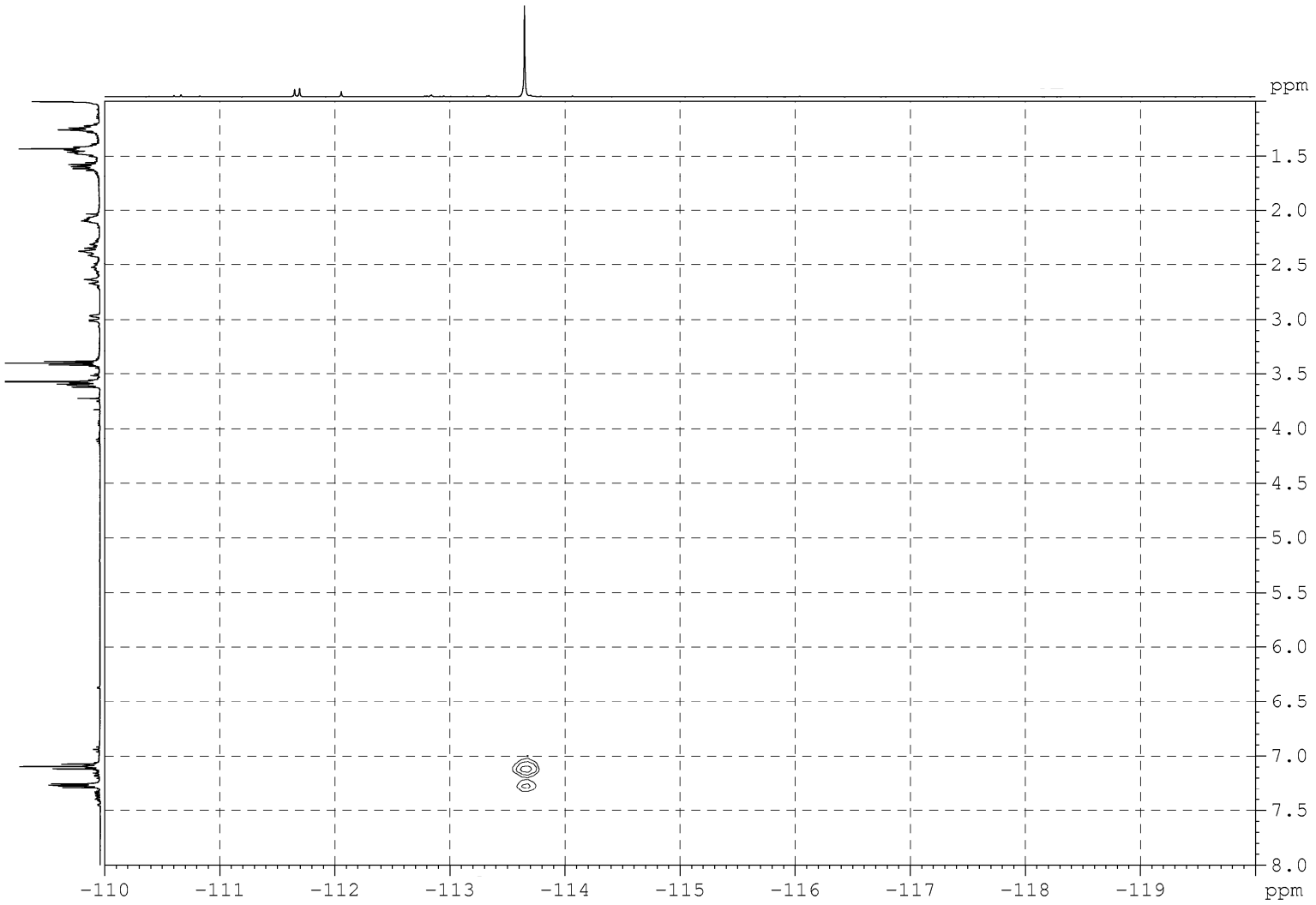

Figure S75. 2D ^{1}H-^{19}F HETCOR NMR spectra of **5i** in $CDCl_3$ at T = 303 K.

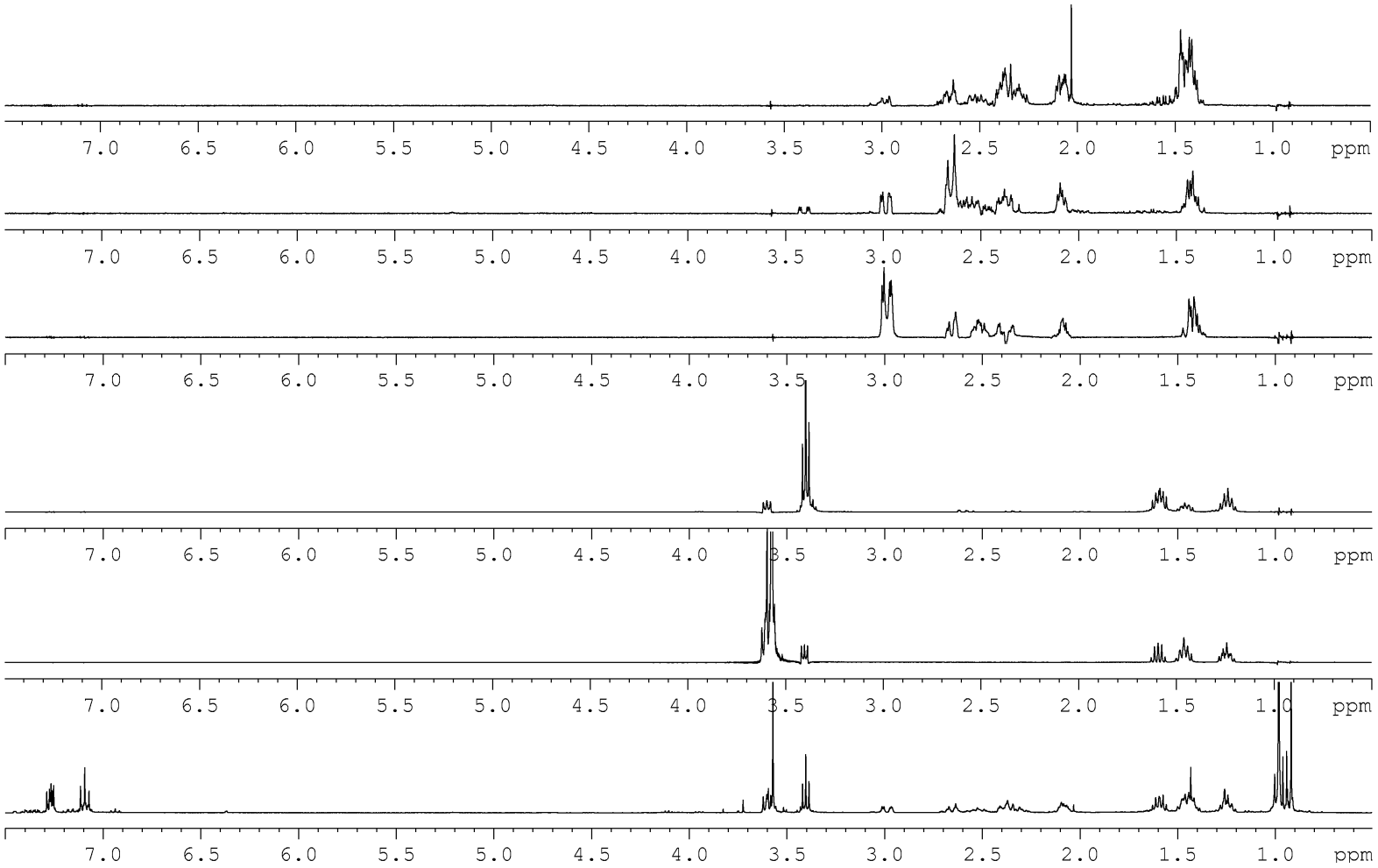

Figure S76. 1D ^{1}H and ^{1}H TOCSY NMR spectra of **5i** in $CDCl_3$ at T = 303 K.

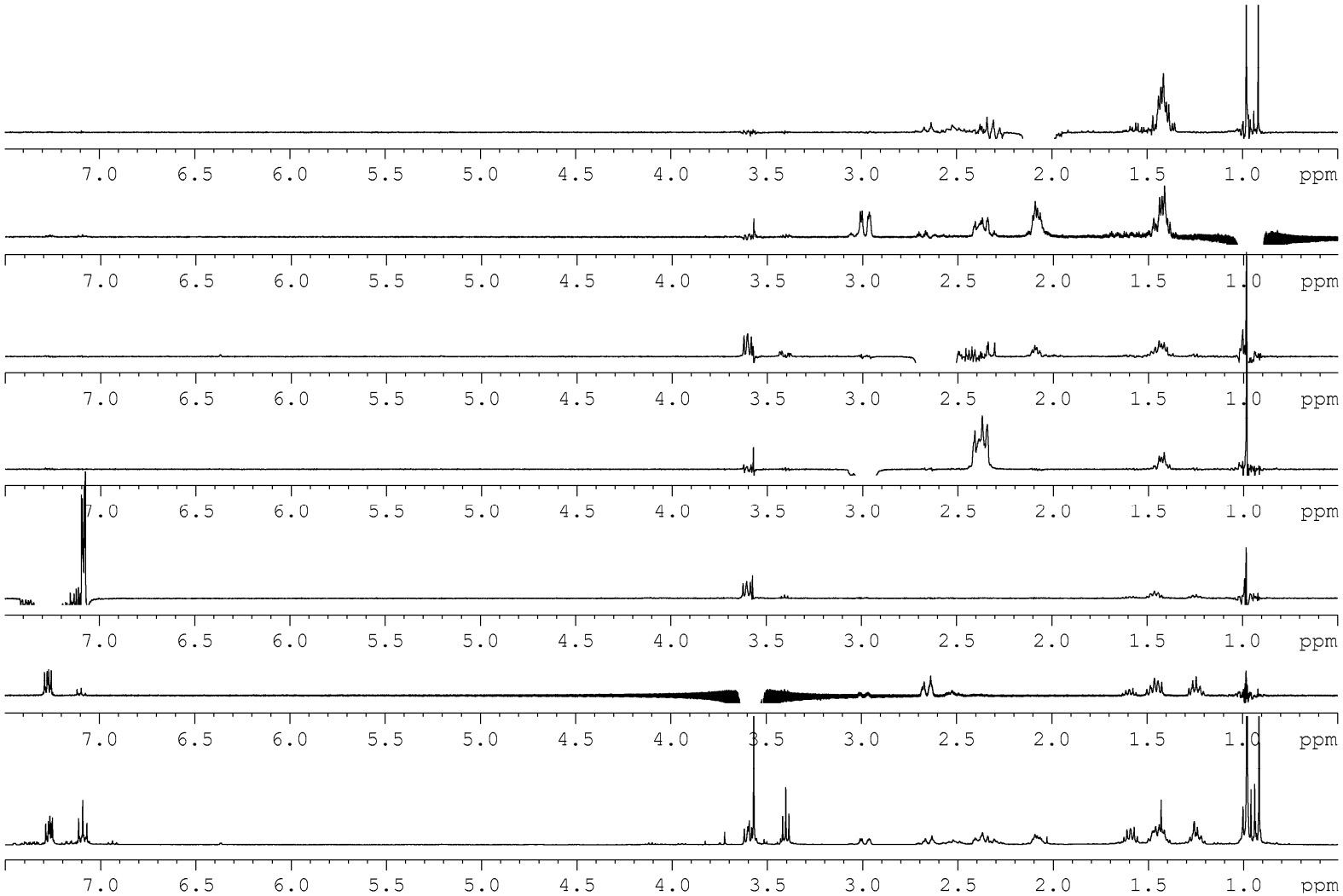

Figure S77. 1D ^{1}H and ^{1}H DPFGROE NMR spectra of **5i** in $CDCl_3$ at T = 303 K.

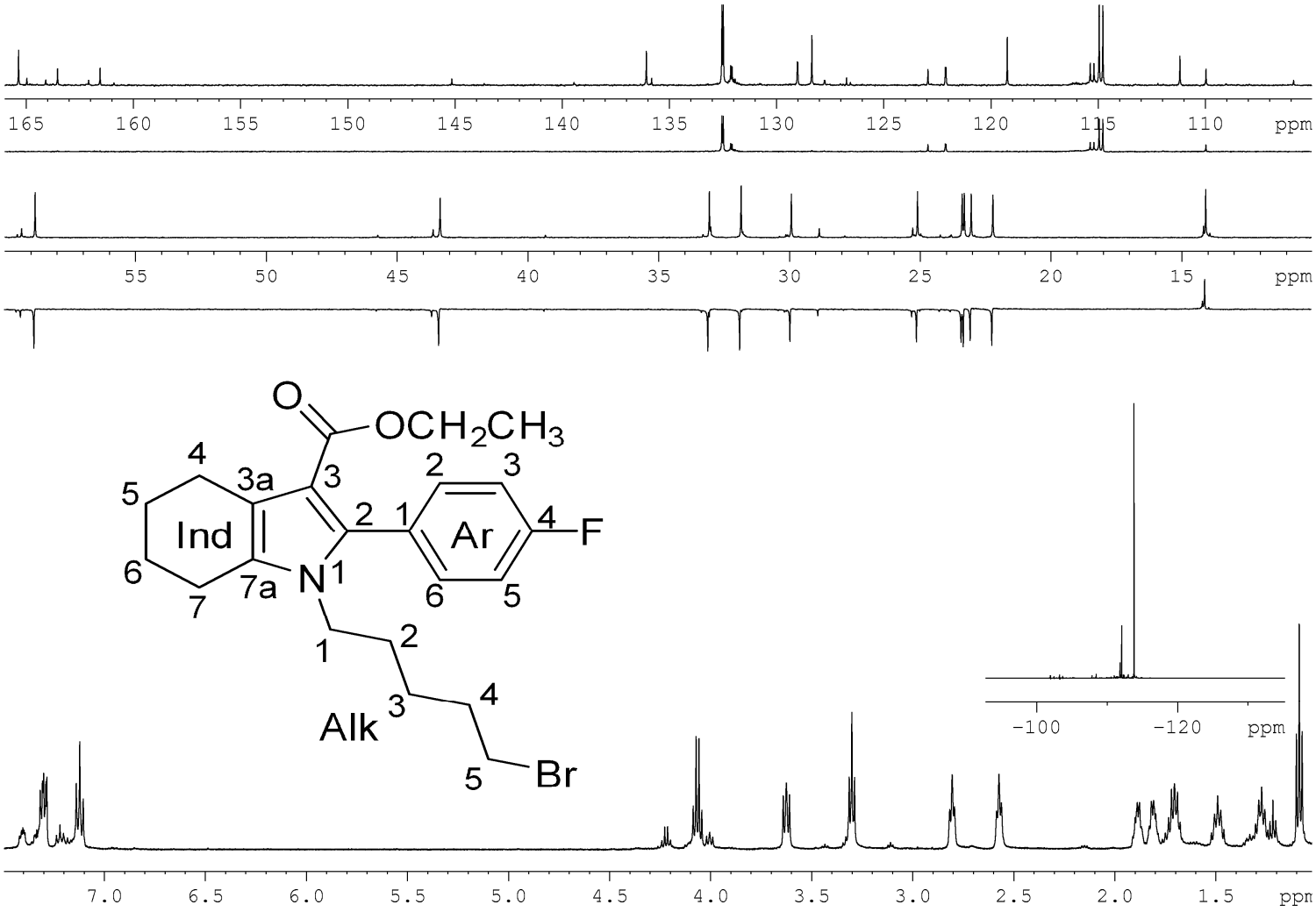

Figure S78. 1D ^{1}H, ^{13}C DEPT, $^{13}C\{^{1}H\}$ and $^{19}F\{^{1}H\}$ NMR spectra of **5j** in $CDCl_3$ at T = 303 K.

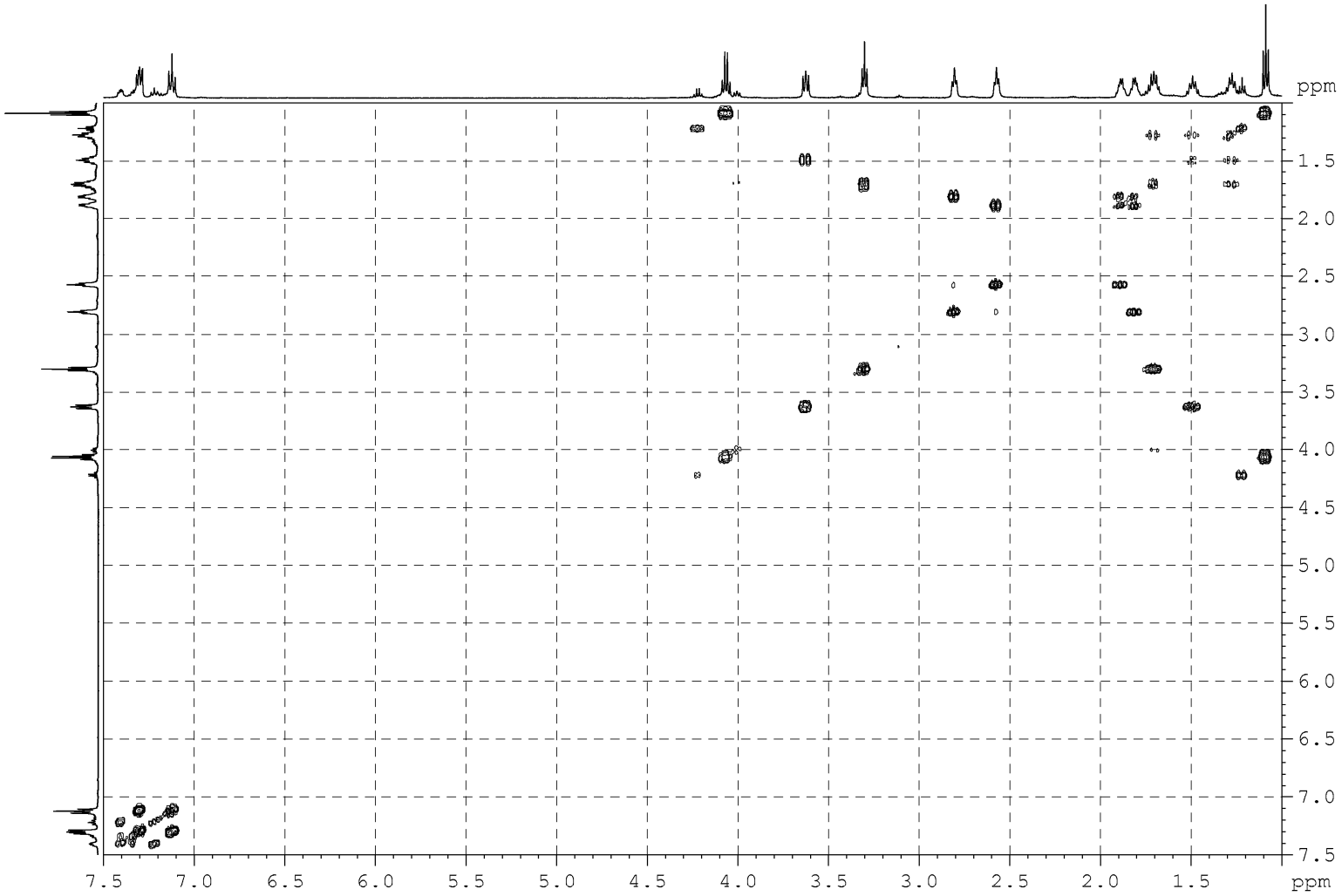

Figure S79. 2D ^{1}H-^{1}H COSY NMR spectra of **5j** in $CDCl_3$ at T = 303 K.

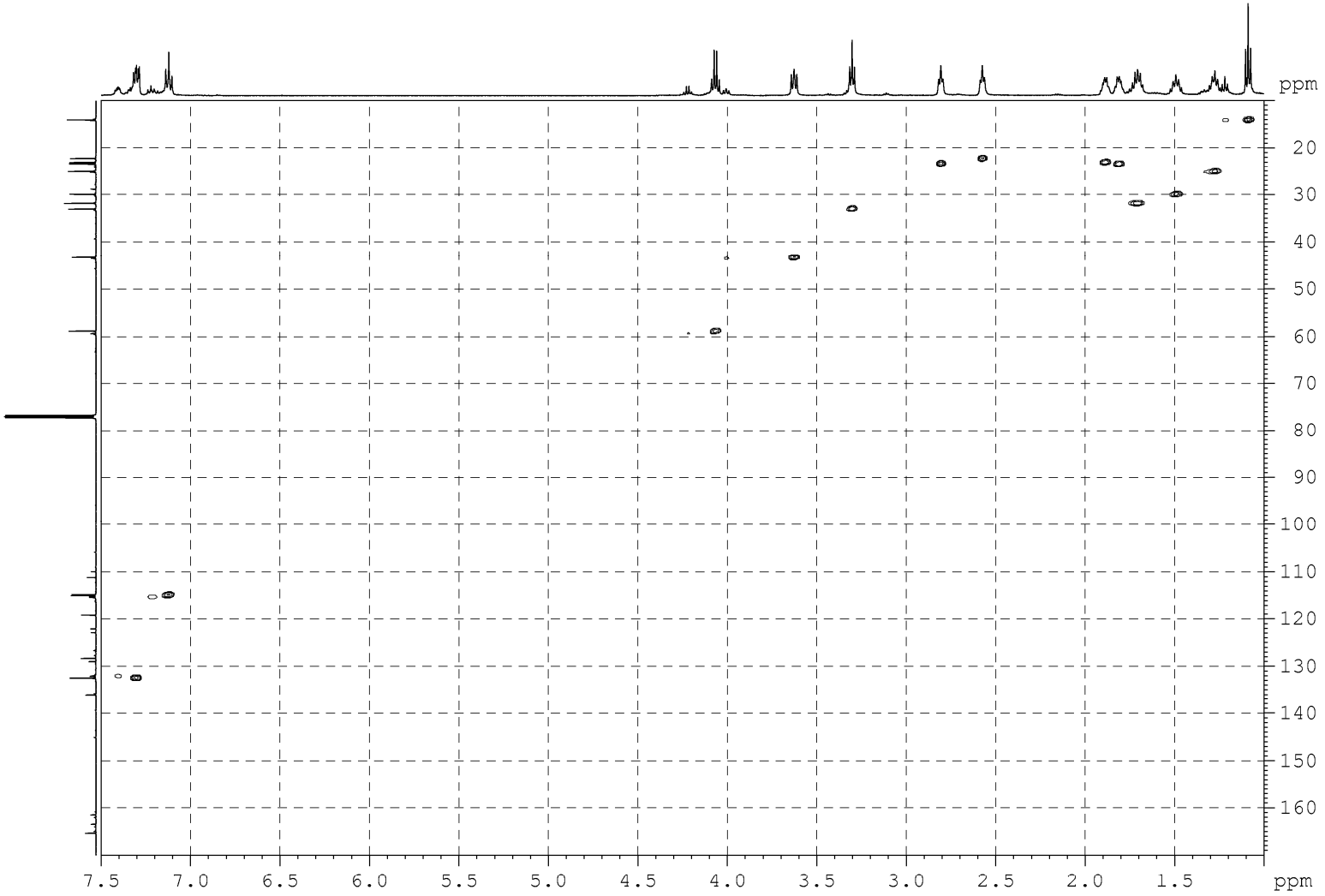

Figure S80. 2D ^{1}H-^{13}C HSQC NMR spectra of **5j** in $CDCl_3$ at T = 303 K.

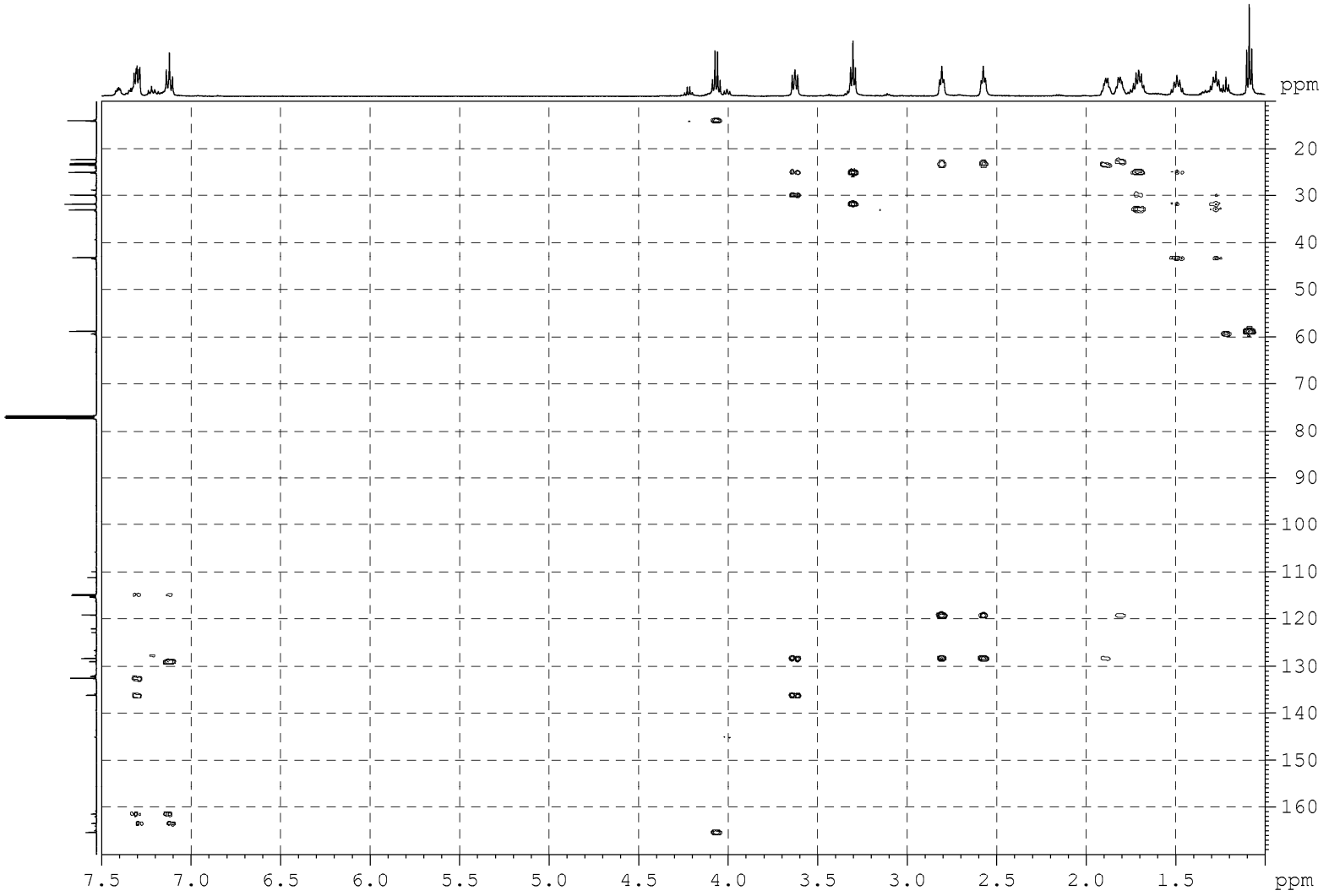

Figure S81. 2D ^{1}H-^{13}C HMBC NMR spectra of **5j** in $CDCl_3$ at T = 303 K.

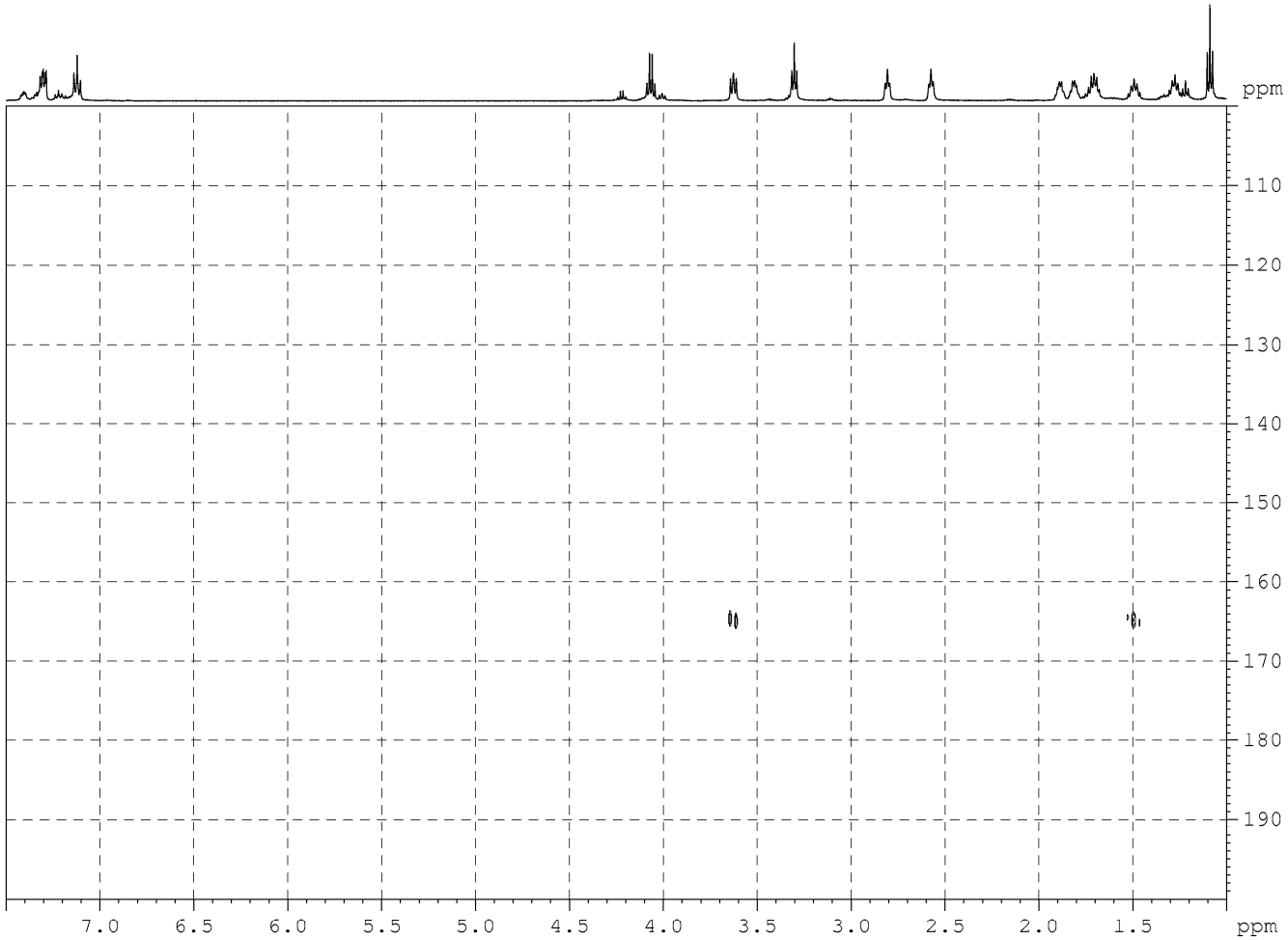

Figure S82. 2D ^{1}H-^{15}N HMBC NMR spectra of **5j** in $CDCl_3$ at T = 303 K.

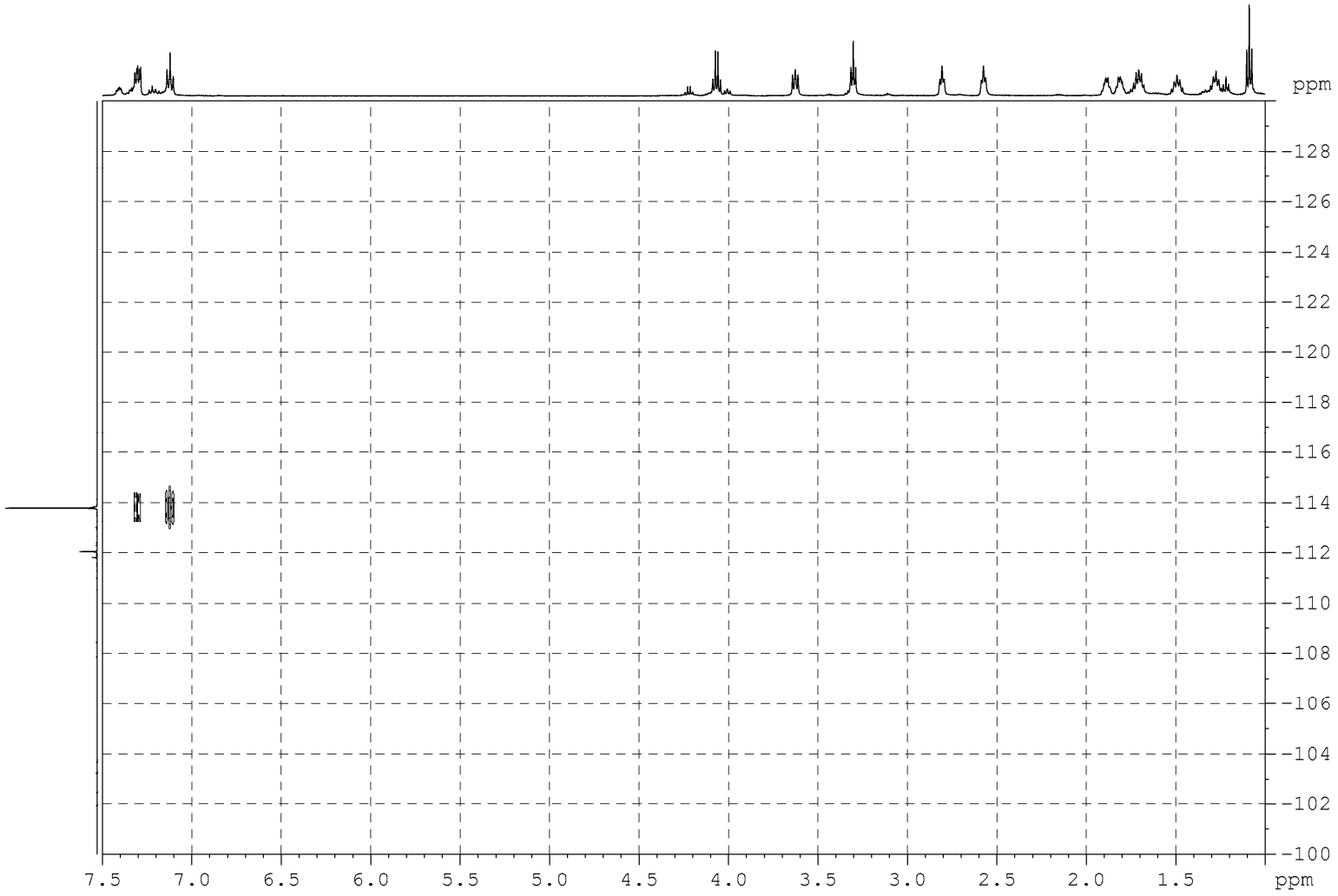

Figure S83. 2D ^{1}H-^{19}F HMBC NMR spectra of **5j** in $CDCl_3$ at T = 303 K.

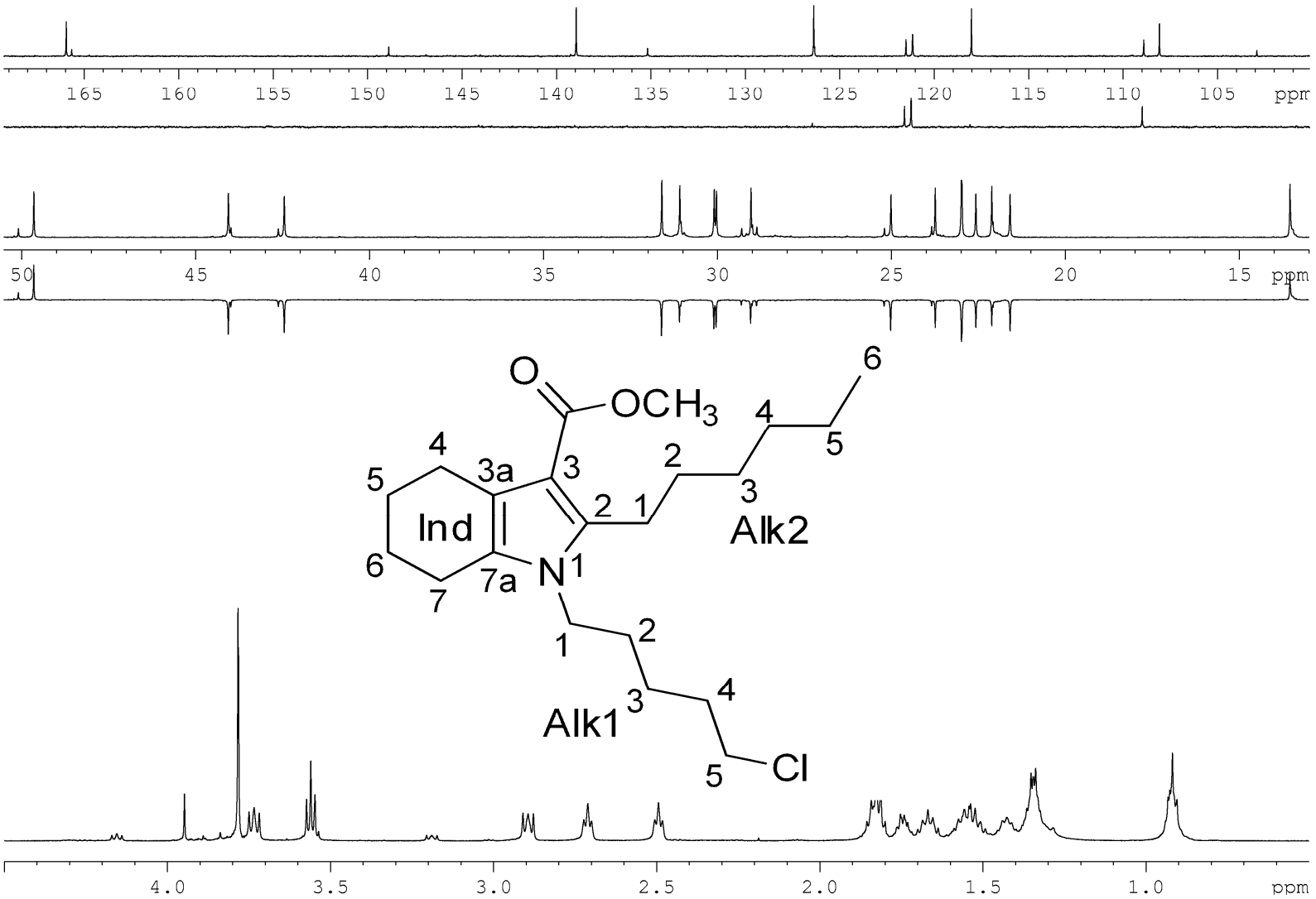

Figure S84. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **5k** in $CDCl_3$ at T = 303 K.

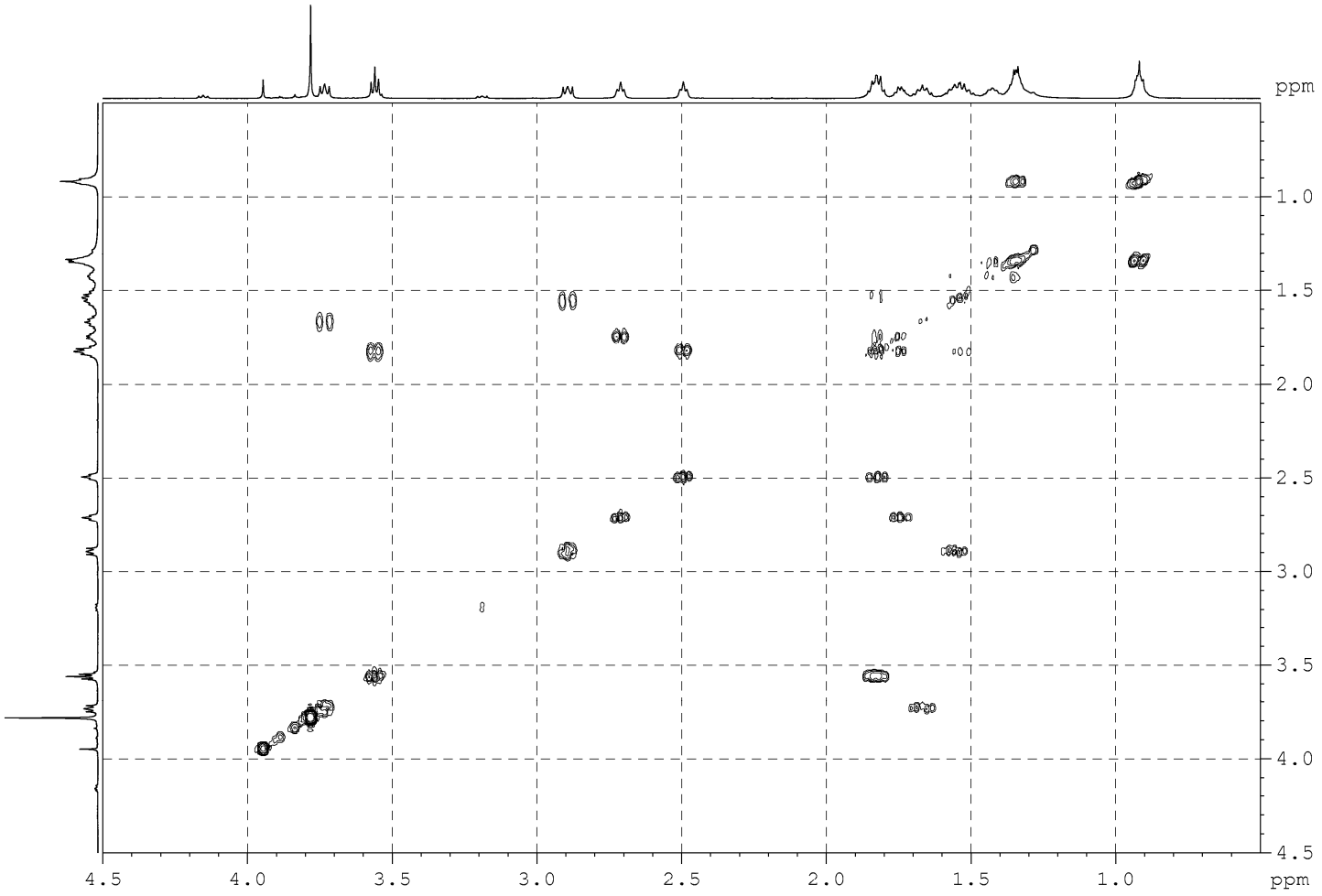

Figure S85. 2D ^{1}H-^{1}H COSY NMR spectra of **5k** in $CDCl_3$ at T = 303 K.

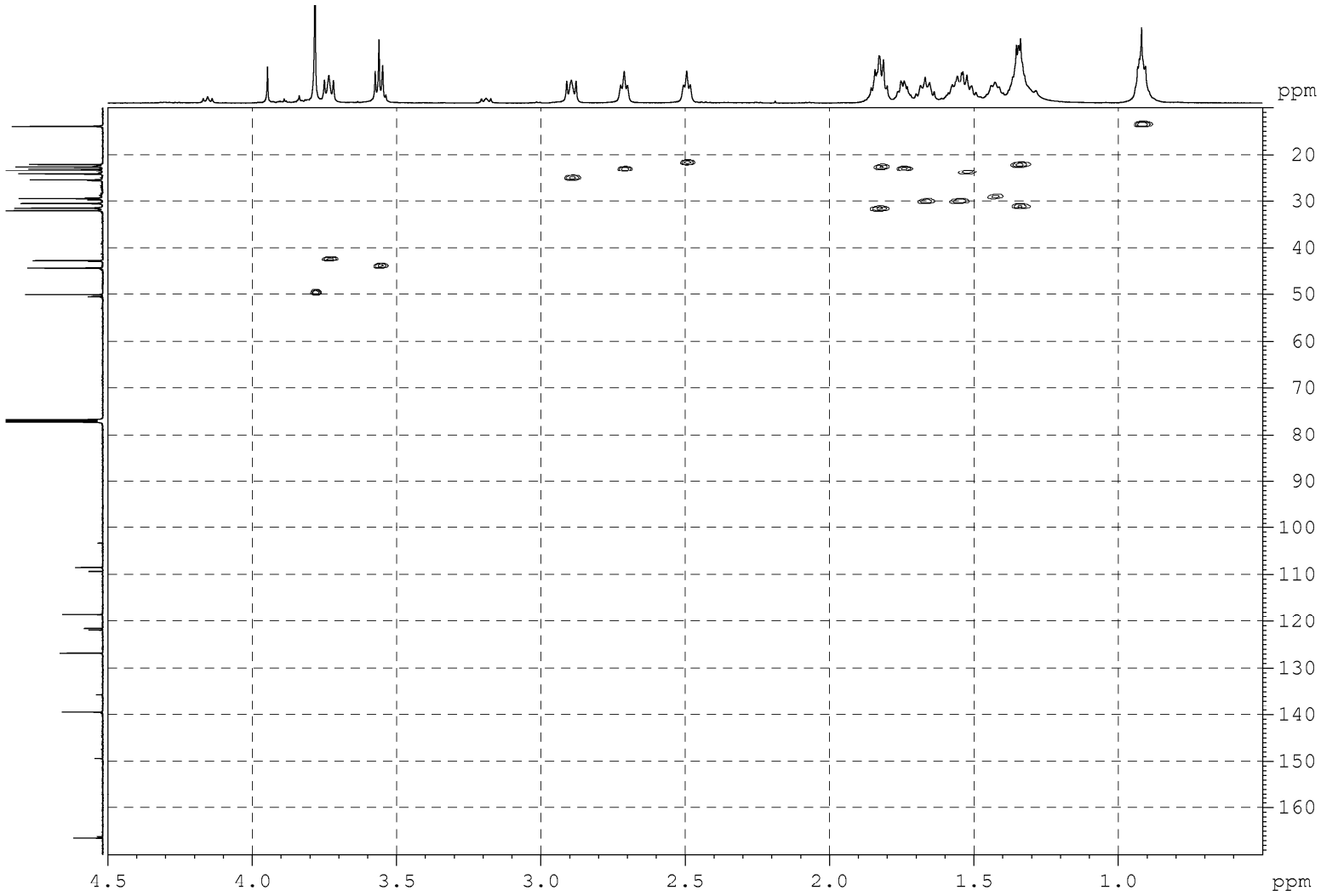

Figure S86. 2D ^{1}H-^{13}C HSQC NMR spectra of **5k** in $CDCl_3$ at T = 303 K.

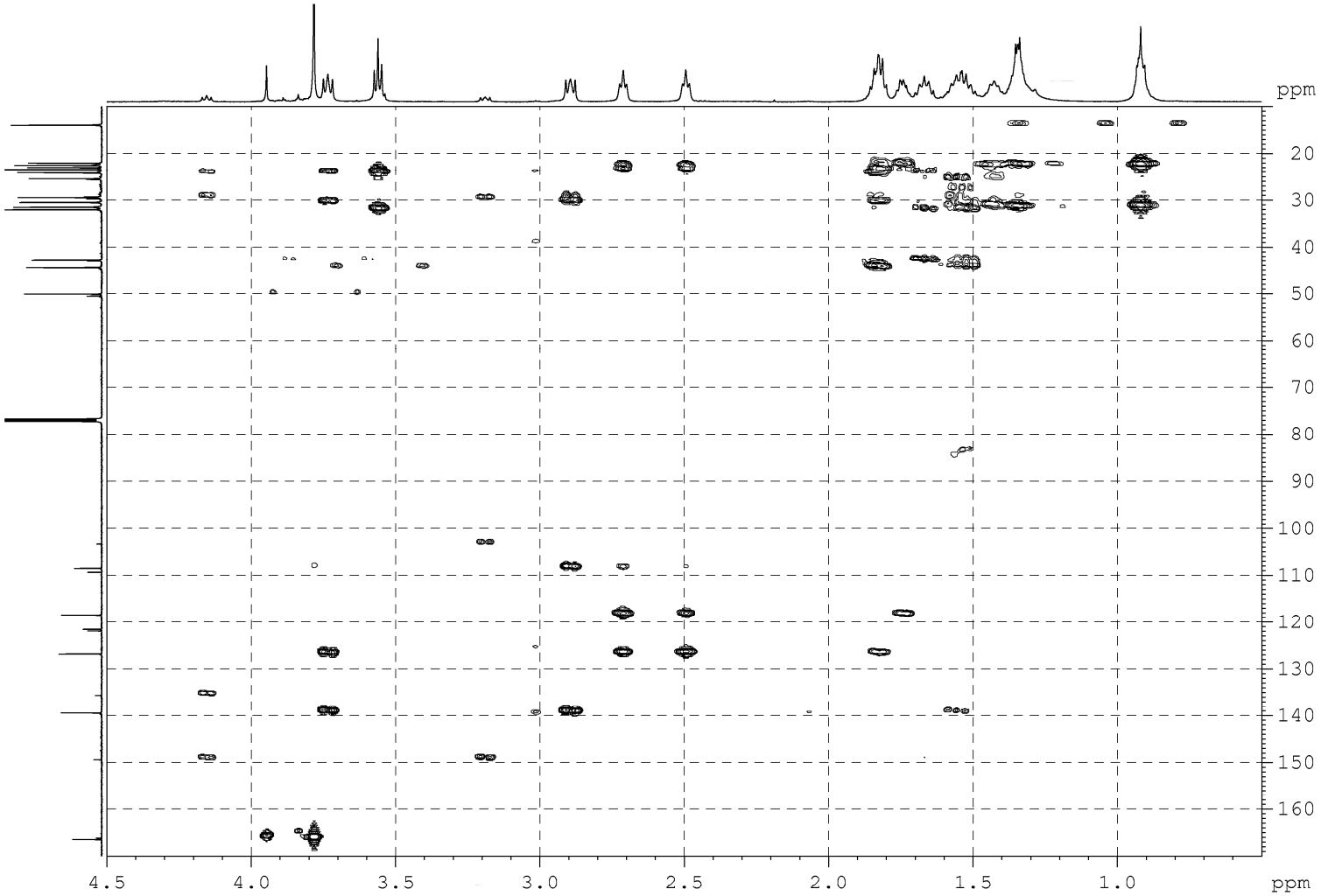

Figure S87. 2D ^{1}H-^{13}C HMBC NMR spectra of **5k** in $CDCl_3$ at T = 303 K.

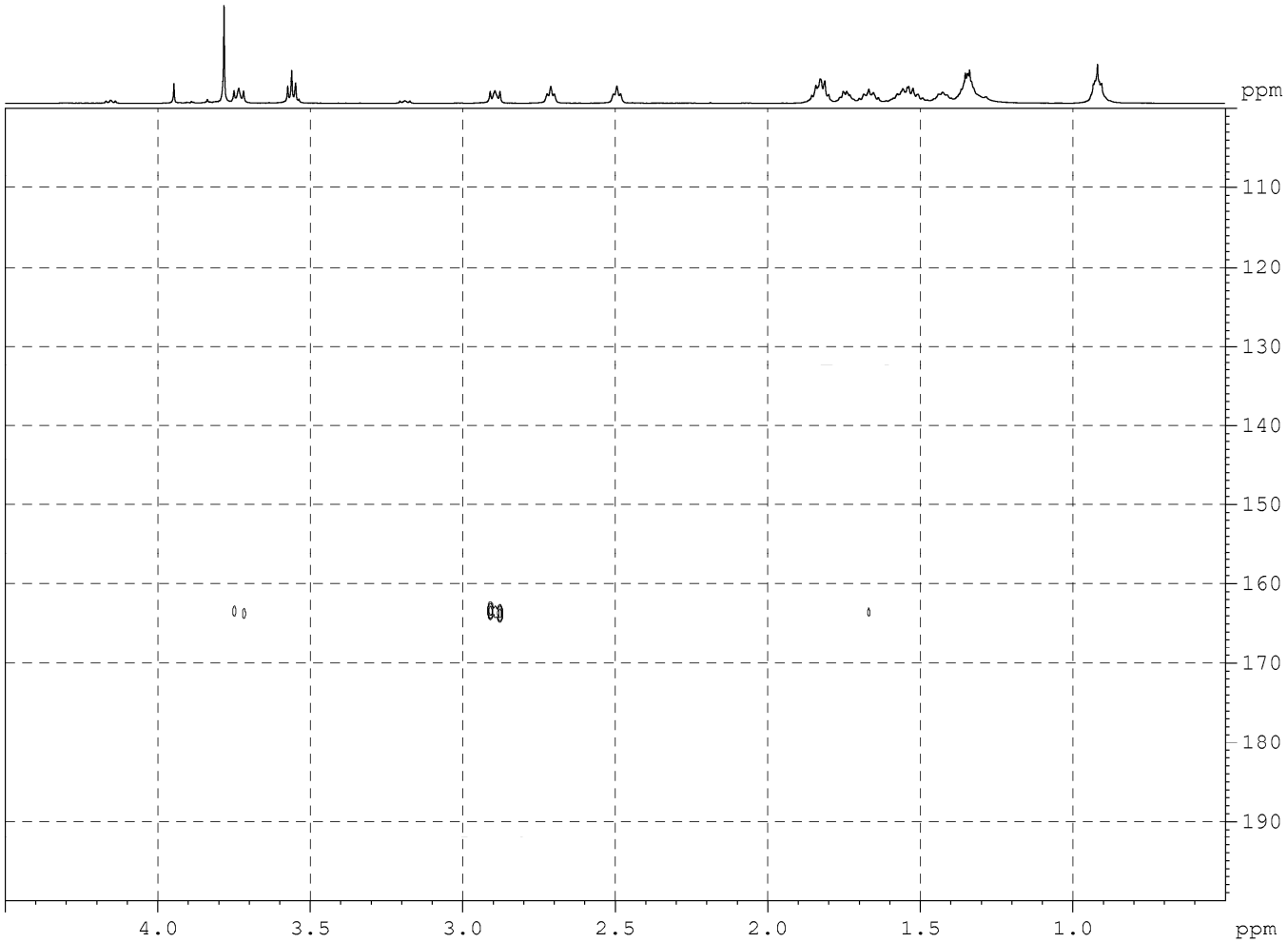

Figure S88. 2D ^{1}H-^{15}N HMBC NMR spectra of **5k** in $CDCl_3$ at T = 303 K.

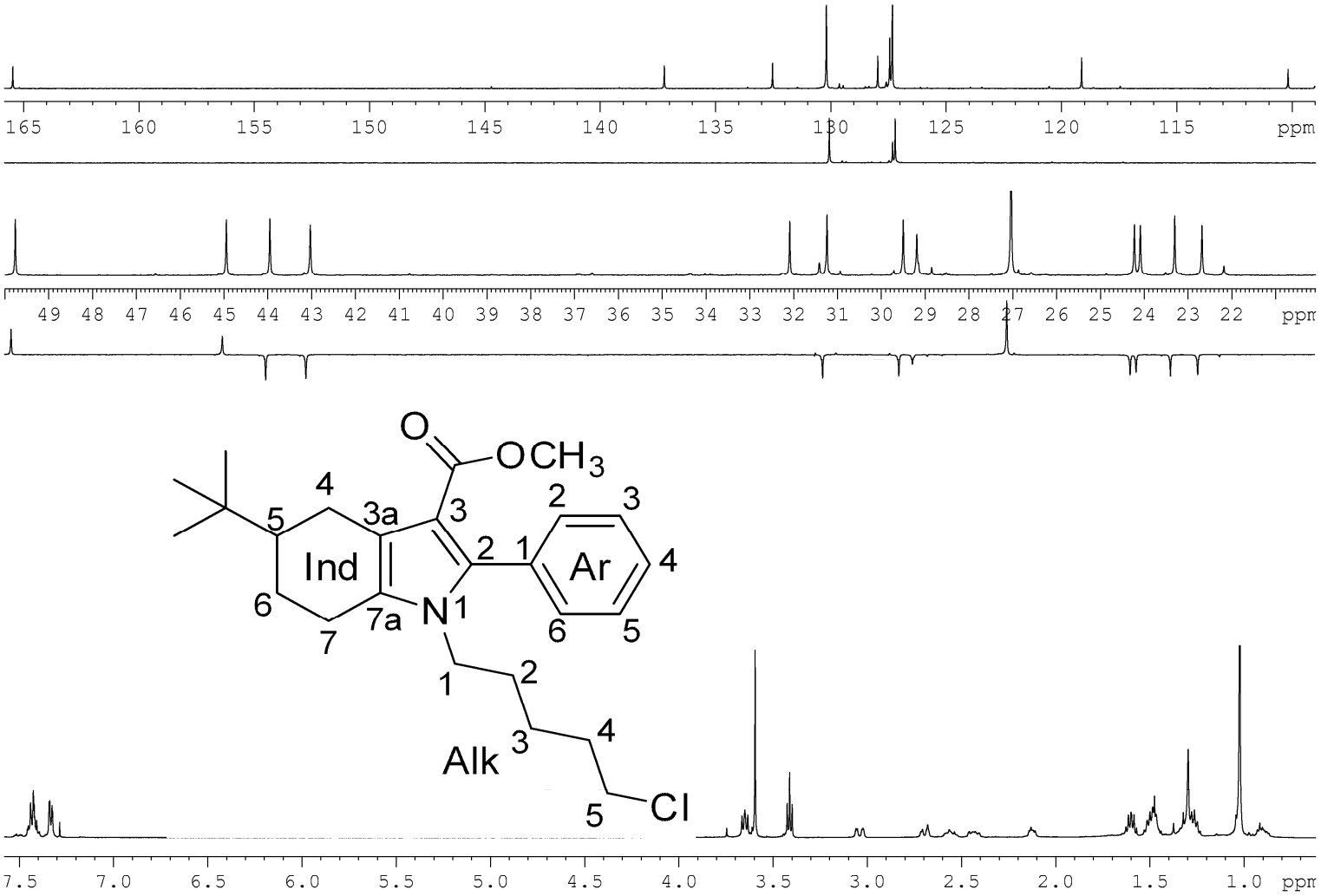

Figure S89. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **5l** in $CDCl_3$ at T = 303 K.

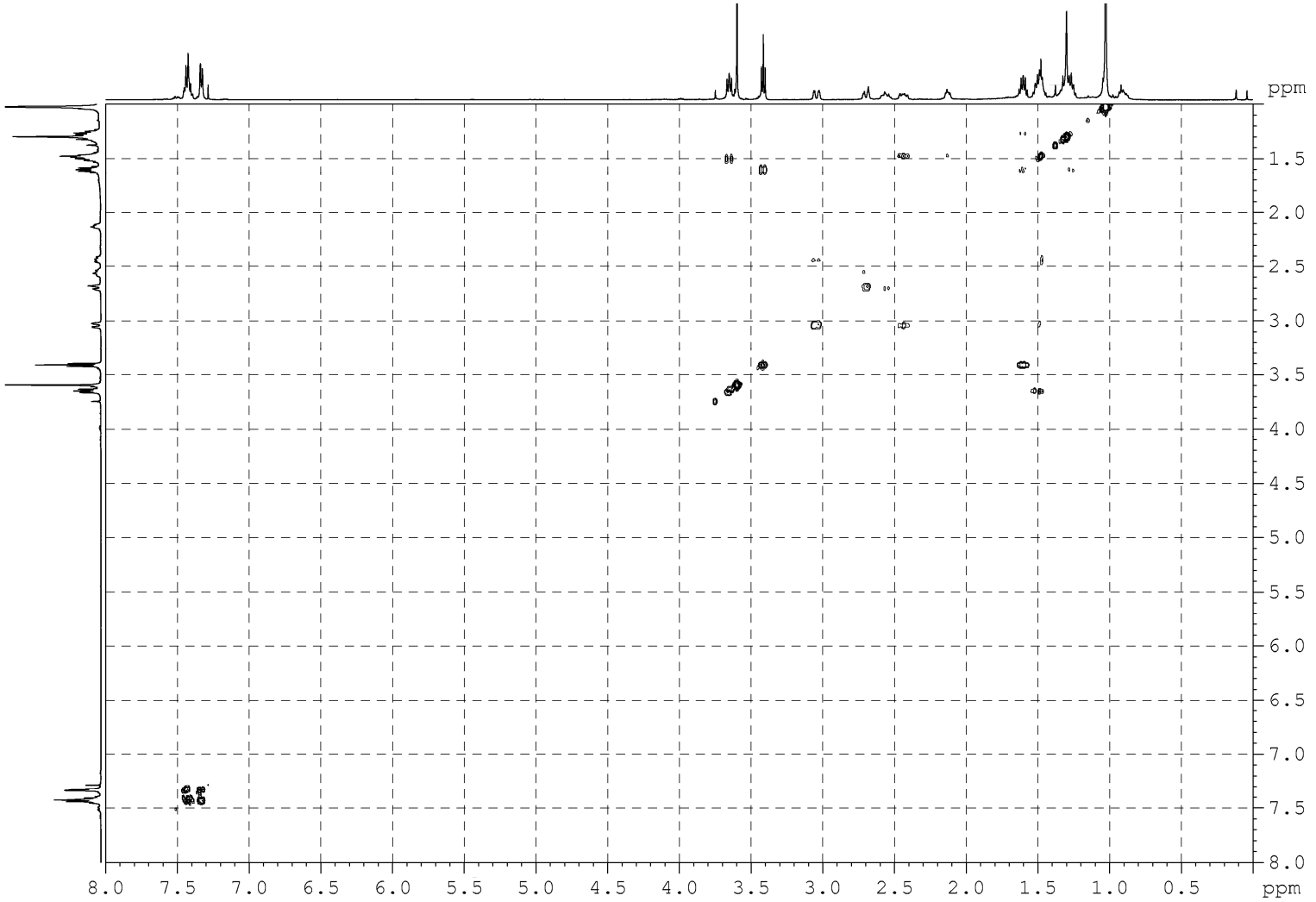

Figure S90. 2D ^{1}H-^{1}H COSY NMR spectra of **5l** in $CDCl_3$ at T = 303 K.

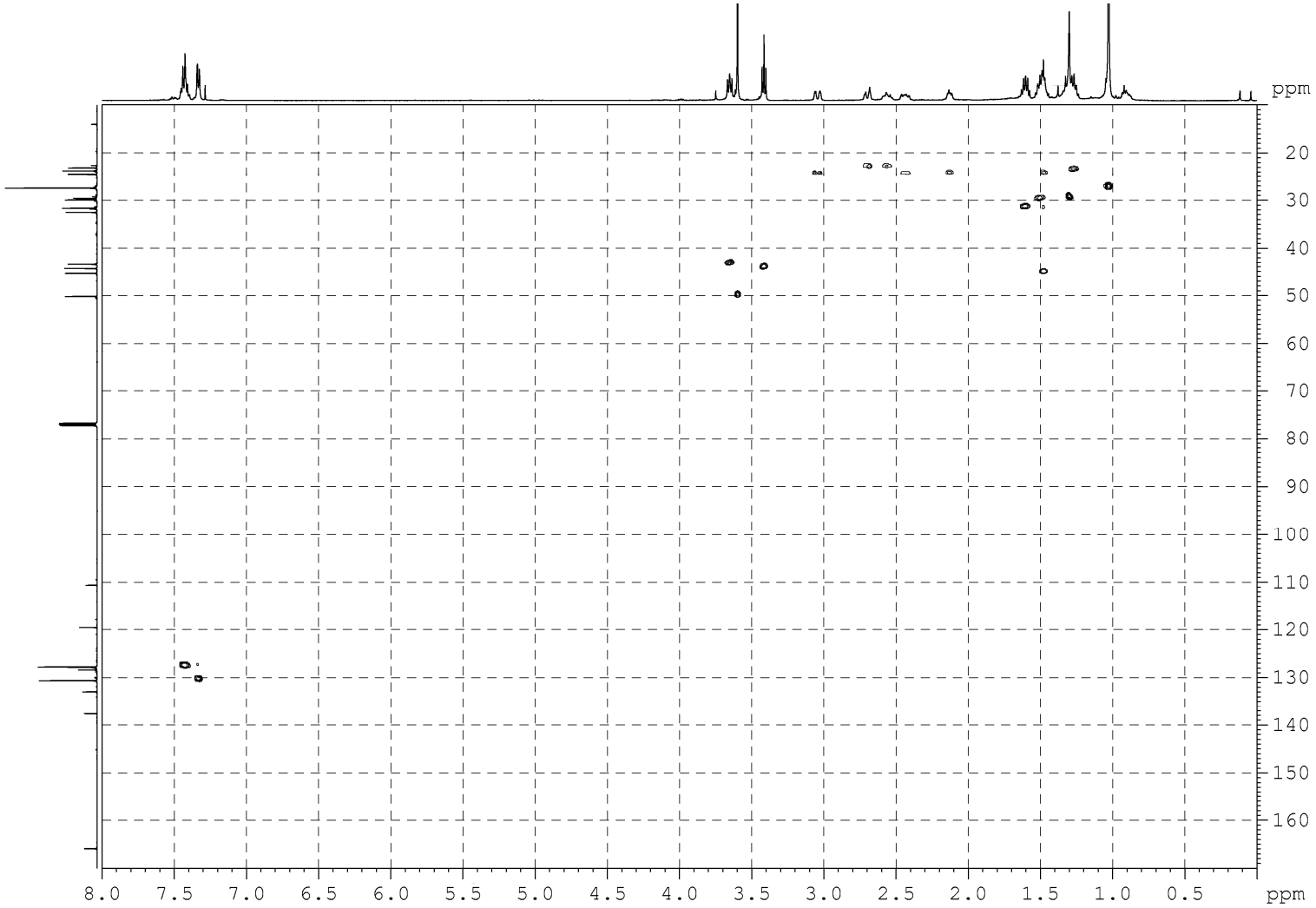

Figure S91. 2D ^{1}H-^{13}C HSQC NMR spectra of **5l** in $CDCl_3$ at T = 303 K.

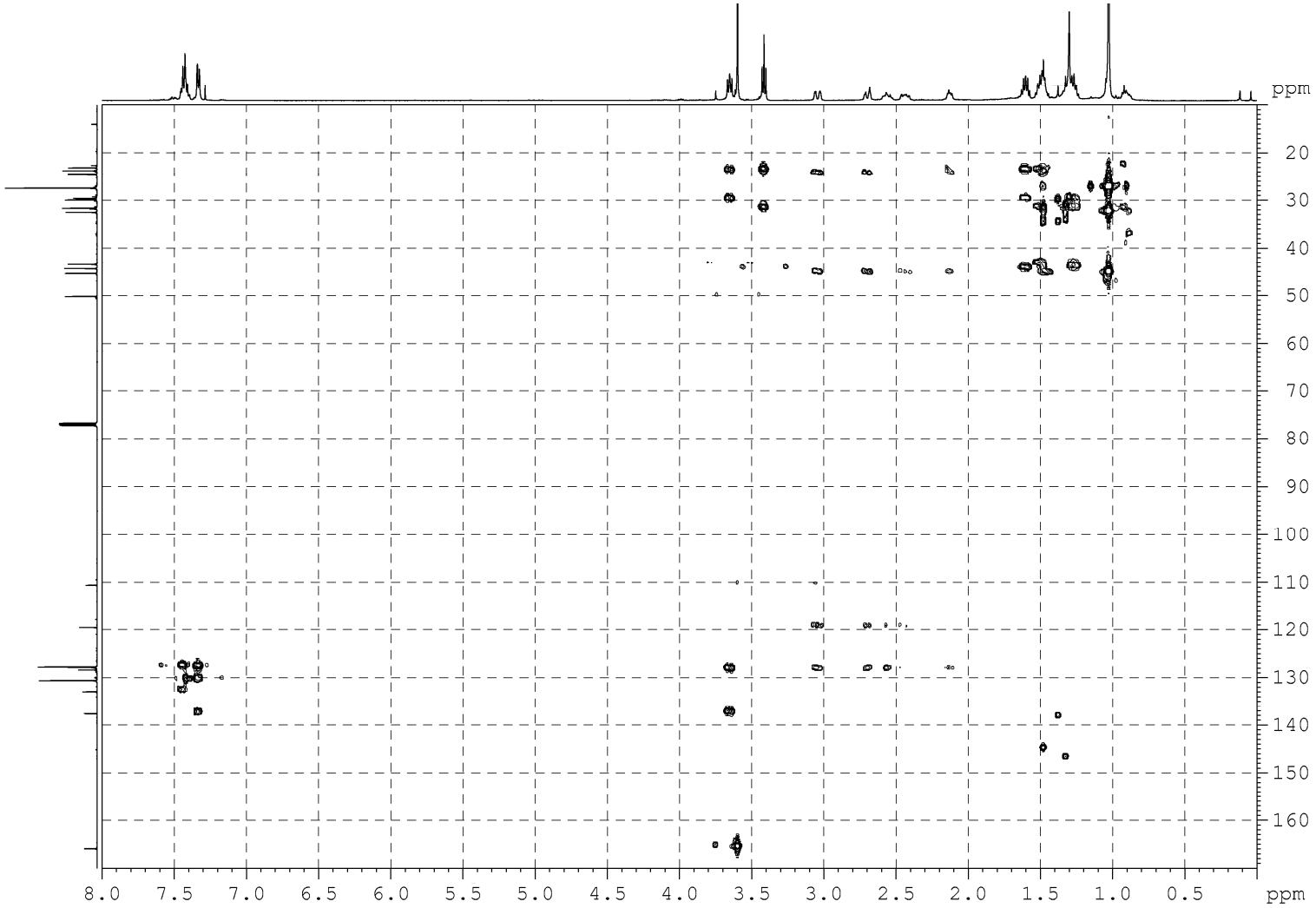

Figure S92. 2D ^{1}H-^{13}C HMBC NMR spectra of **5l** in $CDCl_3$ at T = 303 K.

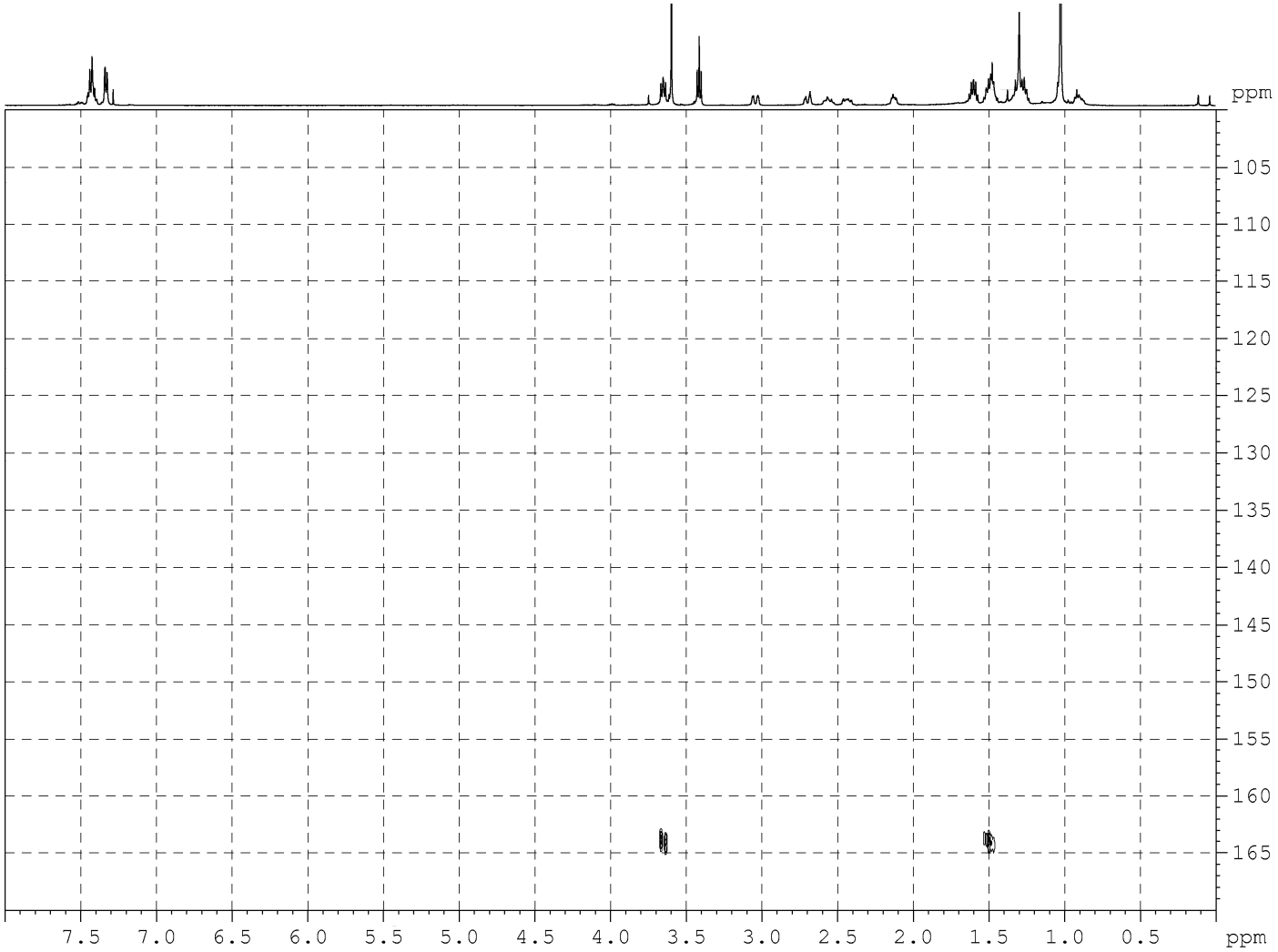

Figure S93. 2D ^{1}H-^{15}N HMBC NMR spectra of **5l** in $CDCl_3$ at T = 303 K.

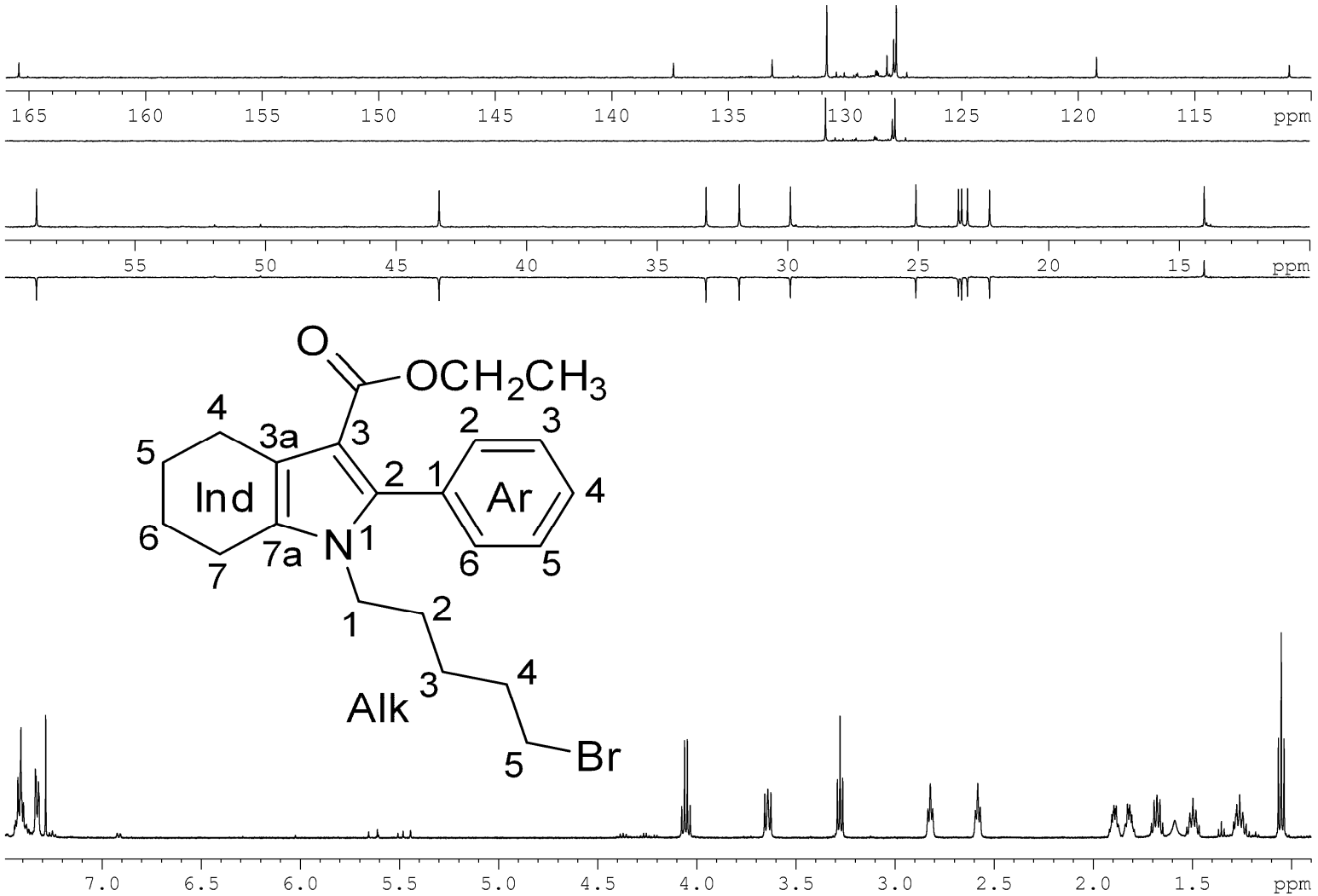

Figure S94. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **5m** in $CDCl_3$ at T = 303 K.

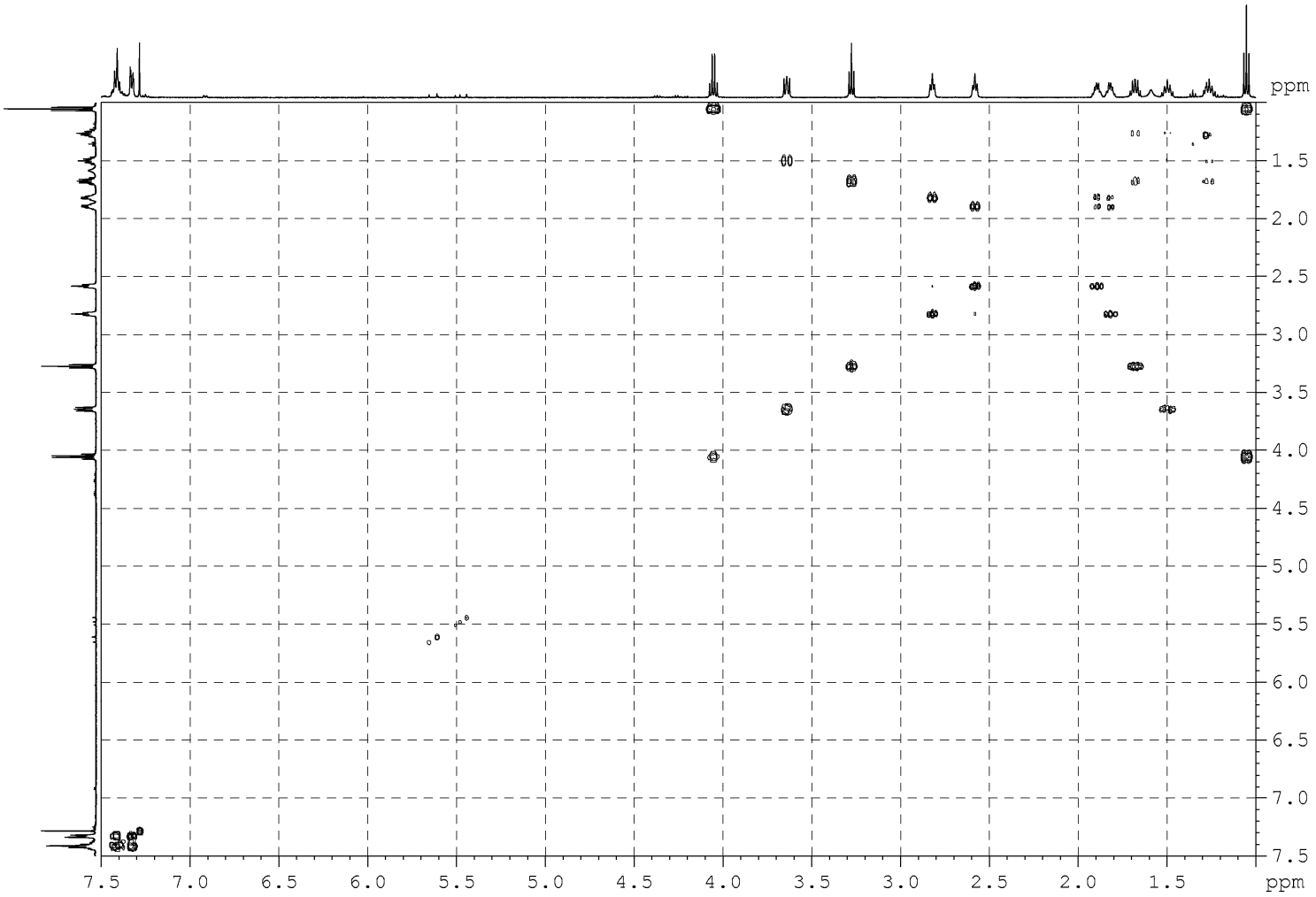

Figure S95. 2D ^{1}H-^{1}H COSY NMR spectra of **5m** in $CDCl_3$ at T = 303 K.

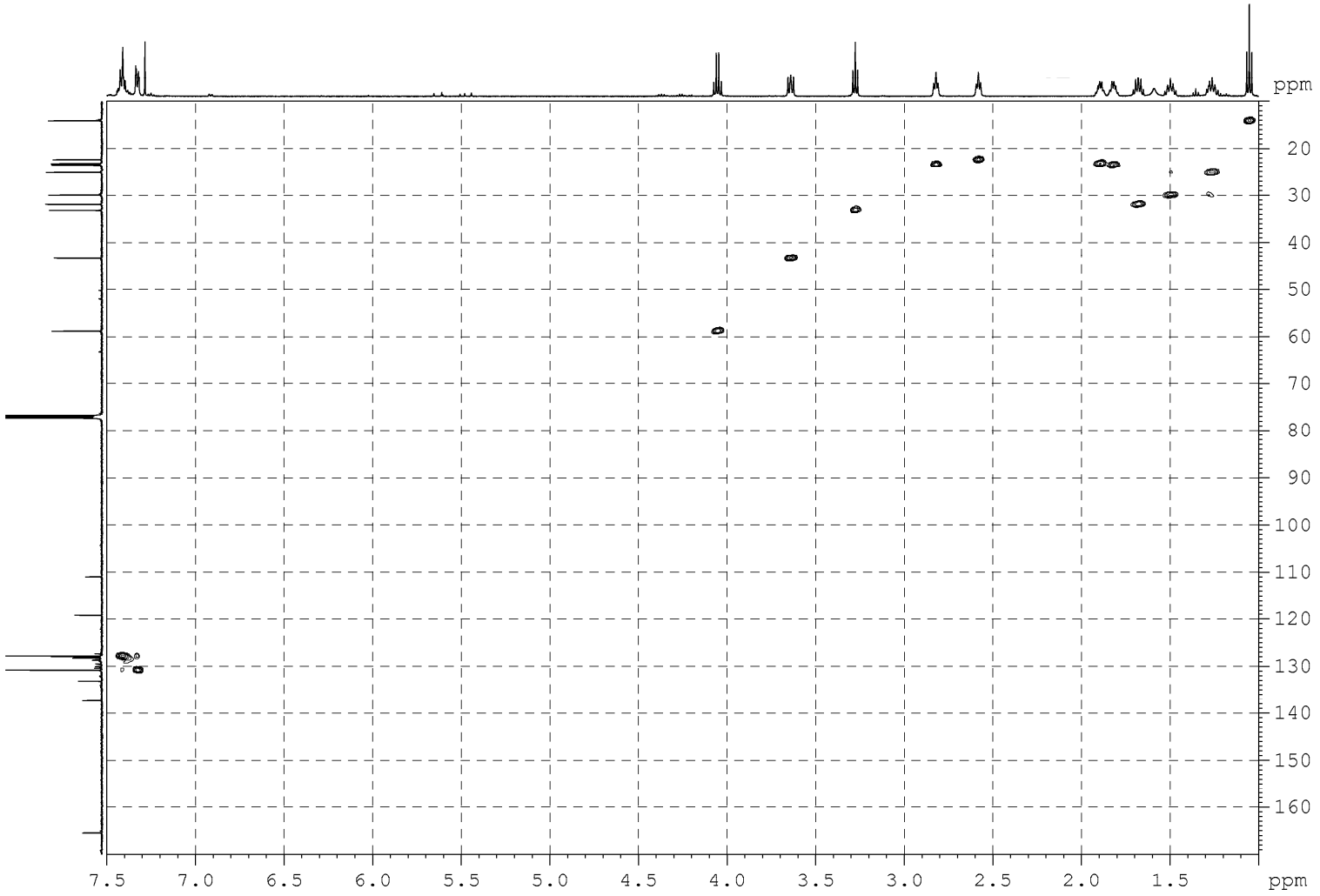

Figure S96. 2D ^{1}H-^{13}C HSQC NMR spectra of **5m** in $CDCl_3$ at T = 303 K.

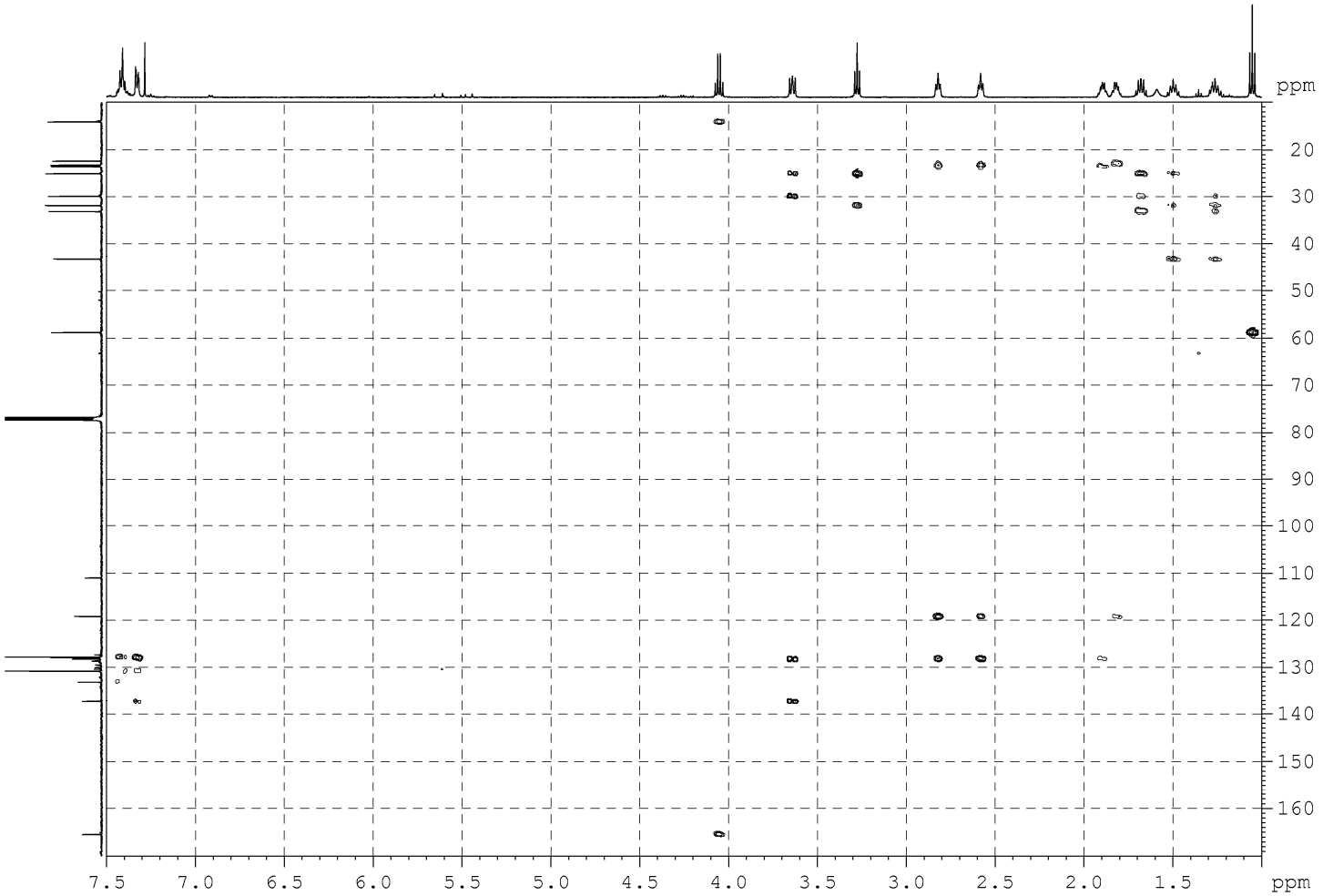

Figure S97. 2D ^{1}H-^{13}C HMBC NMR spectra of **5m** in $CDCl_3$ at T = 303 K.

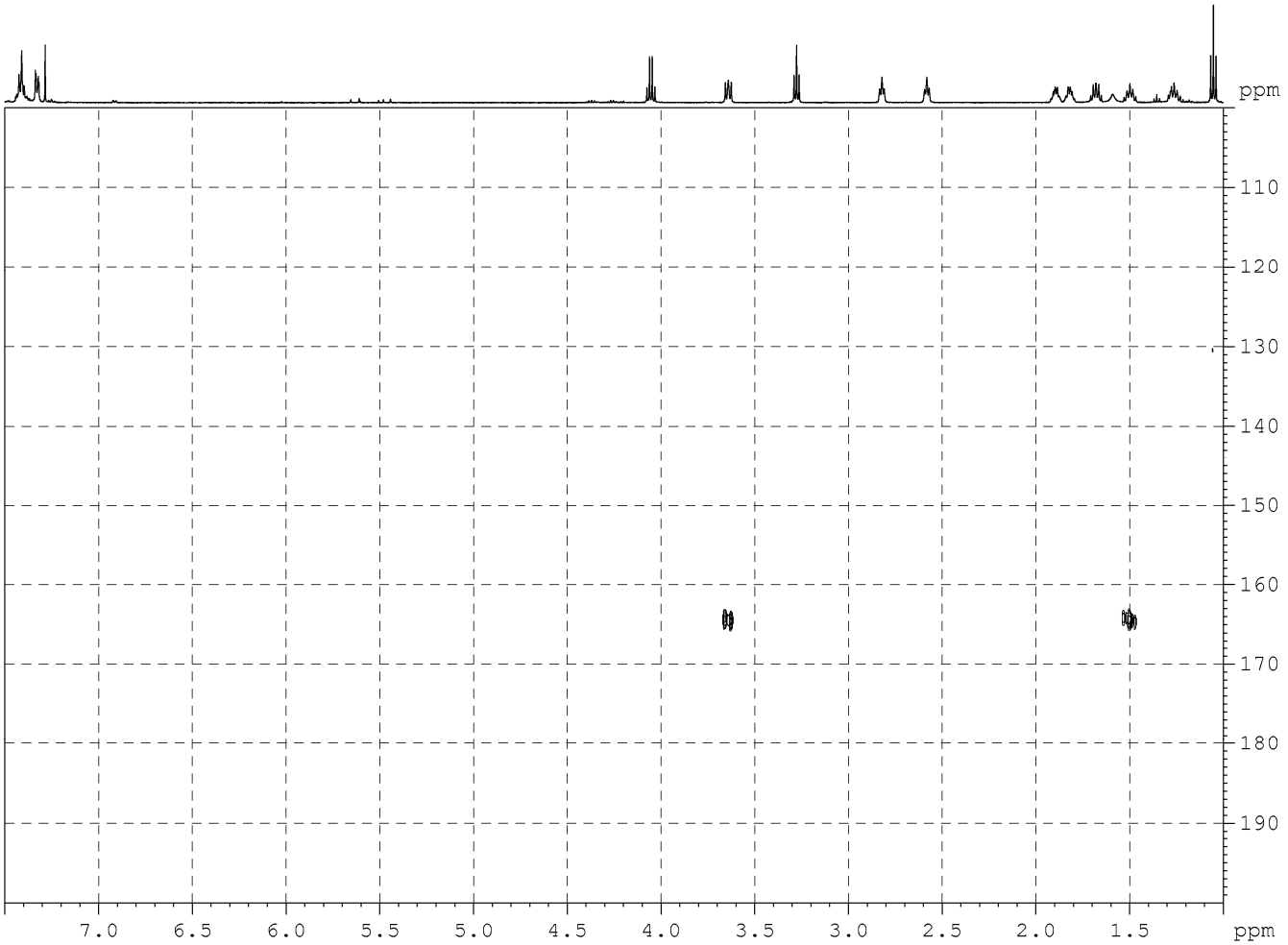

Figure S98. 2D ^{1}H-^{15}N HMBC NMR spectra of **5m** in $CDCl_3$ at T = 303 K.

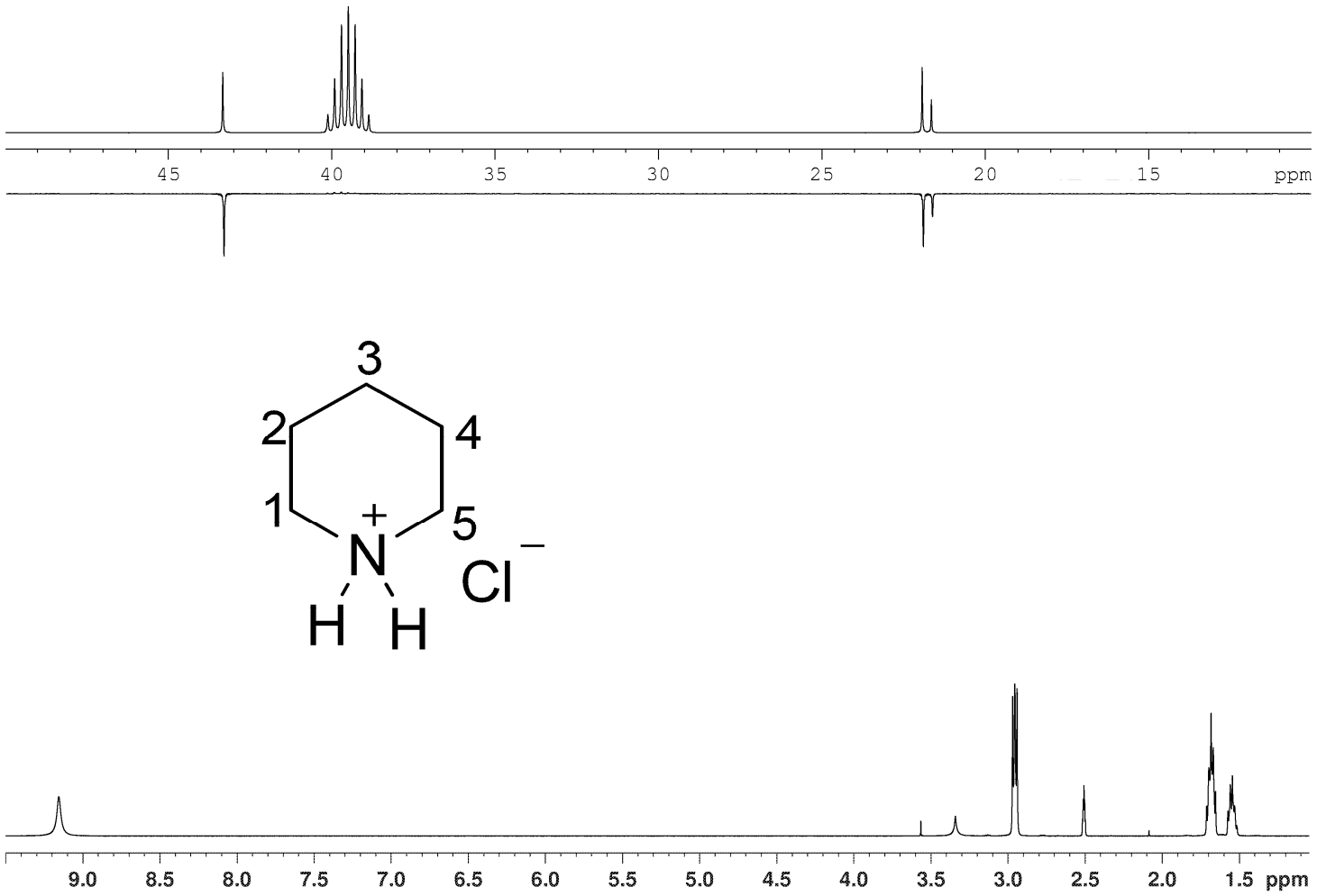

Figure S99. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **6a** in DMSO at T = 303 K.

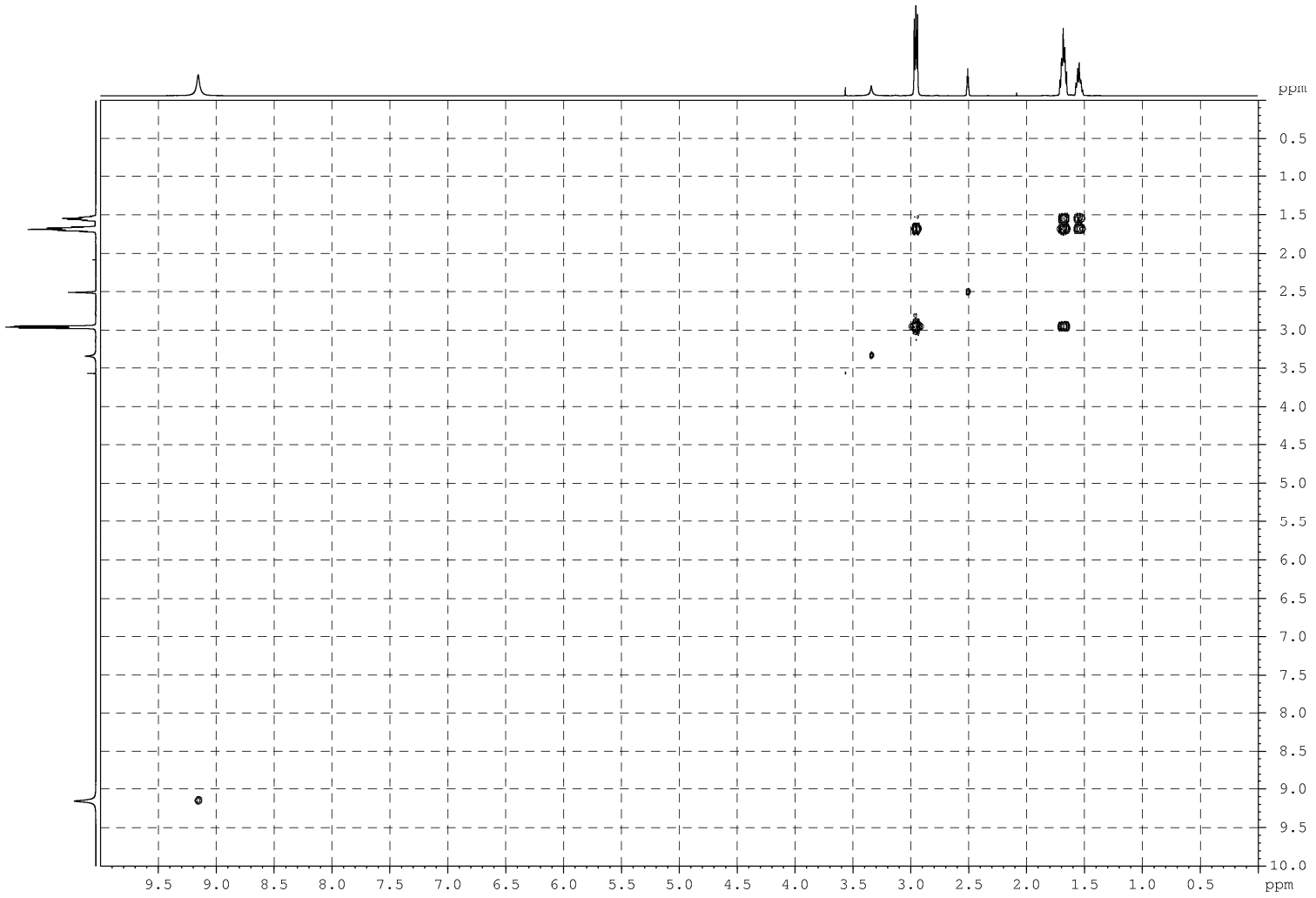

Figure S100. 2D ^{1}H-^{1}H COSY NMR spectra of **6a** in DMSO at T = 303 K.

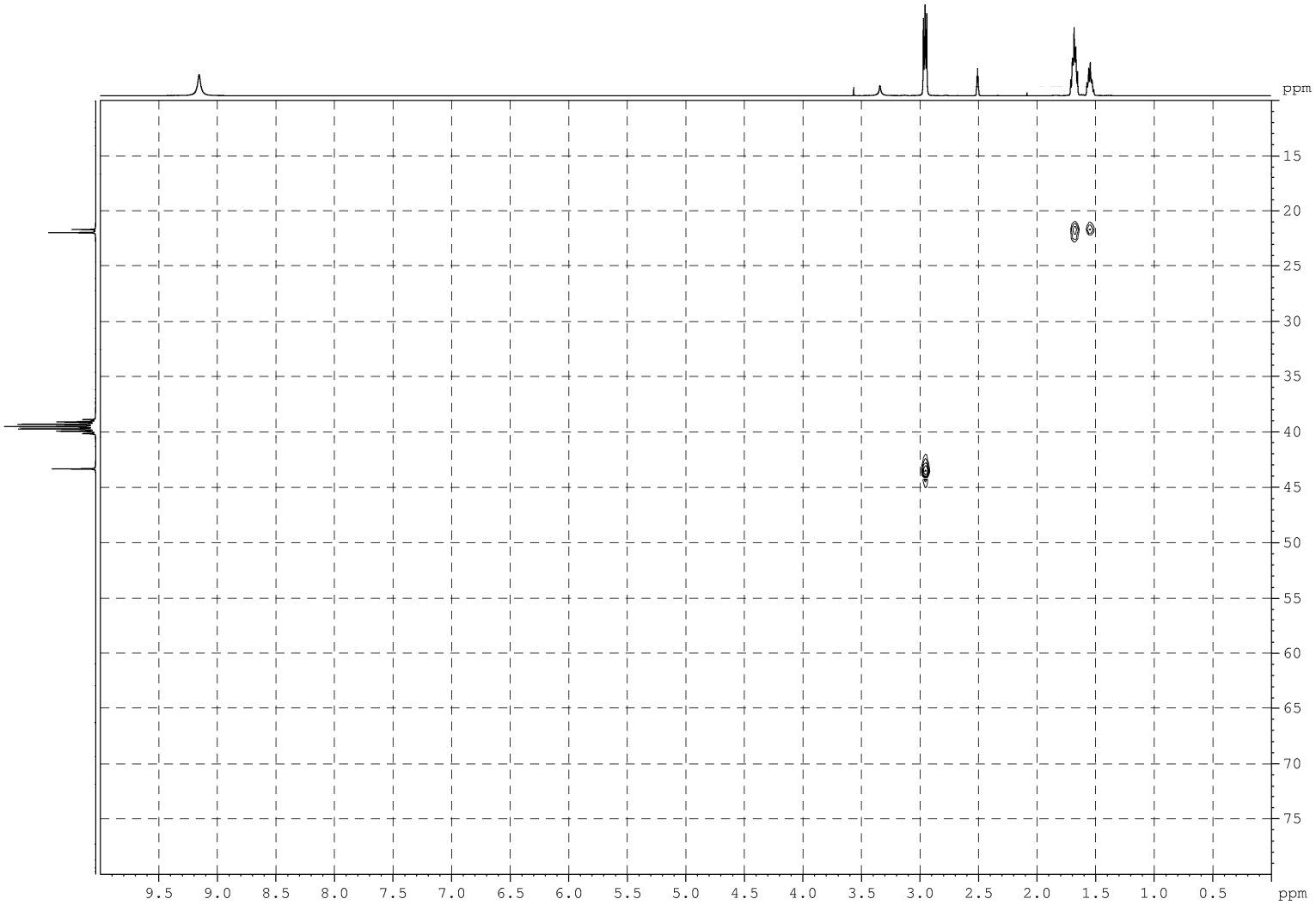

Figure S101. 2D ^{1}H-^{13}C HSQC NMR spectra of **6a** in DMSO at T = 303 K.

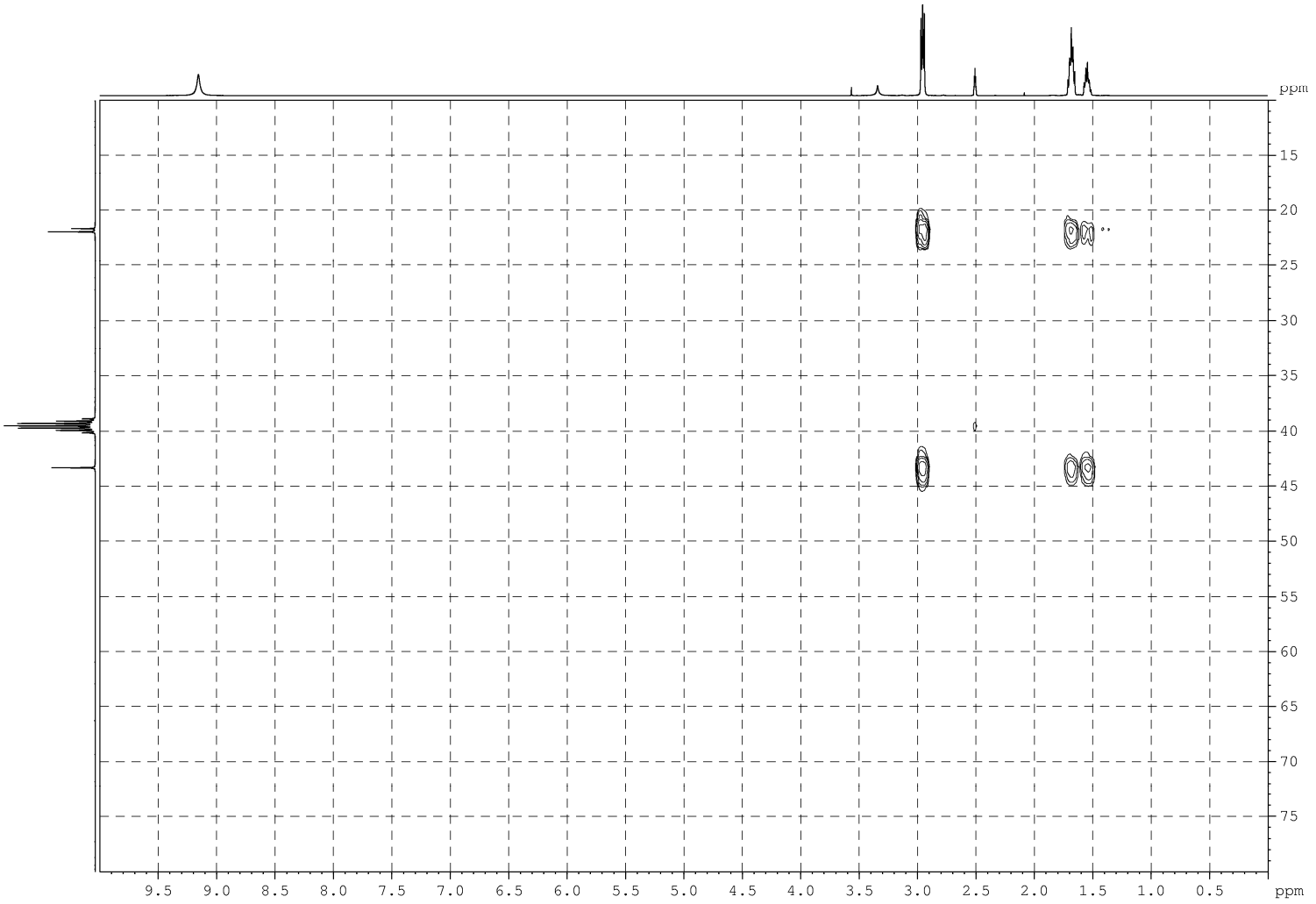

Figure S102. 2D ^{1}H-^{13}C HMBC NMR spectra of **6a** in DMSO at T = 303 K.

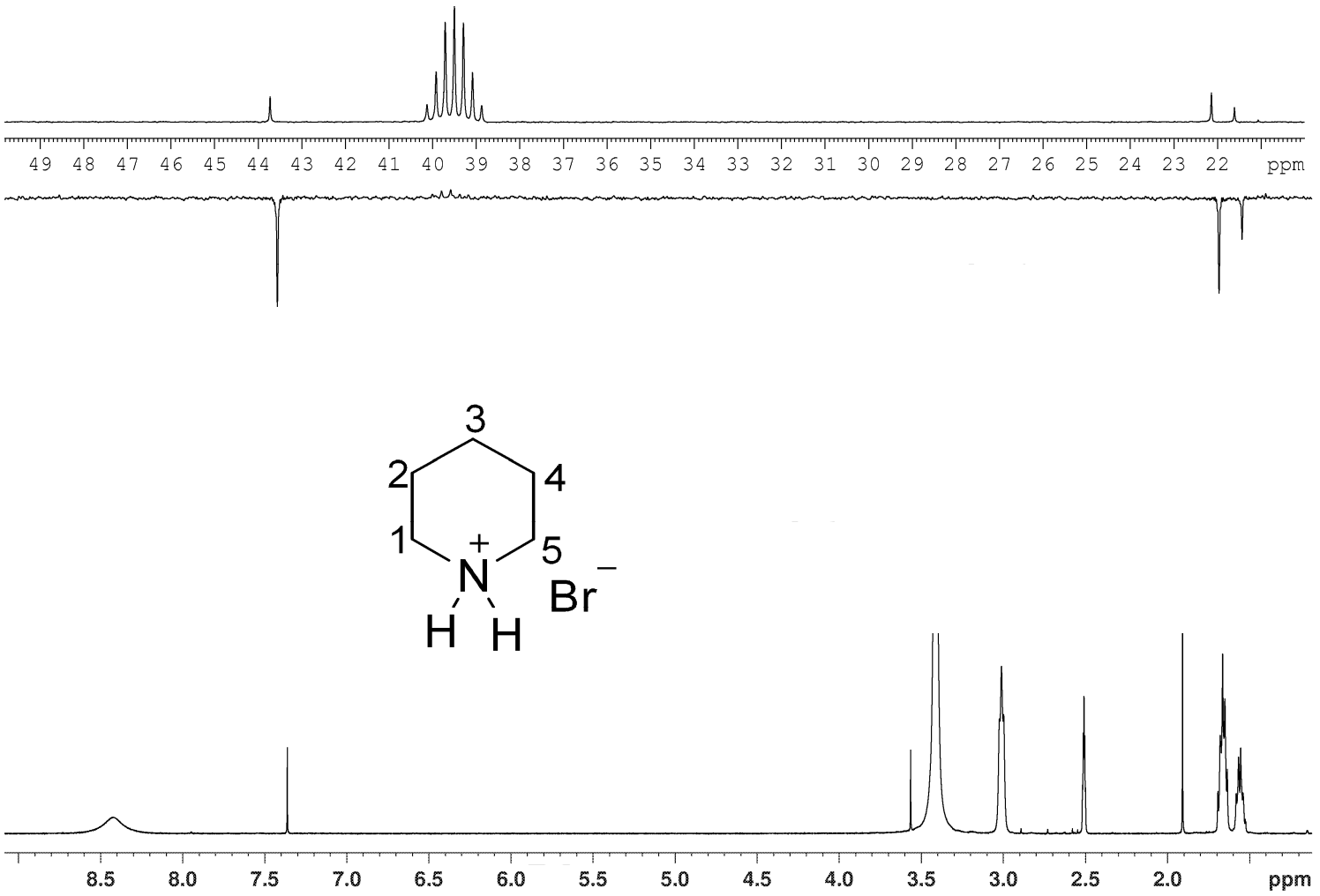

Figure S103. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **6b** in DMSO at T = 303 K.

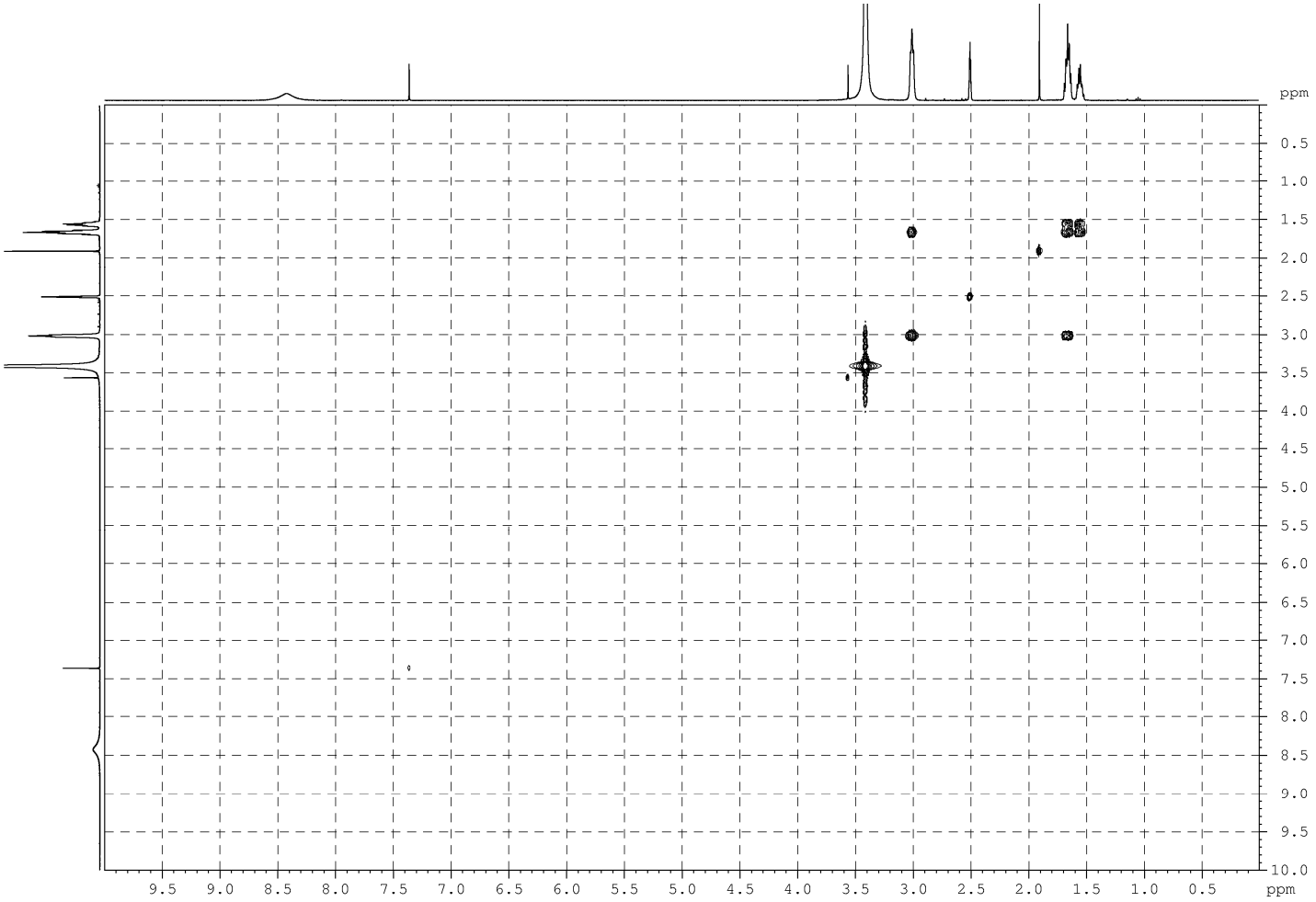

Figure S104. 2D ^{1}H-^{1}H COSY NMR spectra of **6b** in DMSO at T = 303 K.

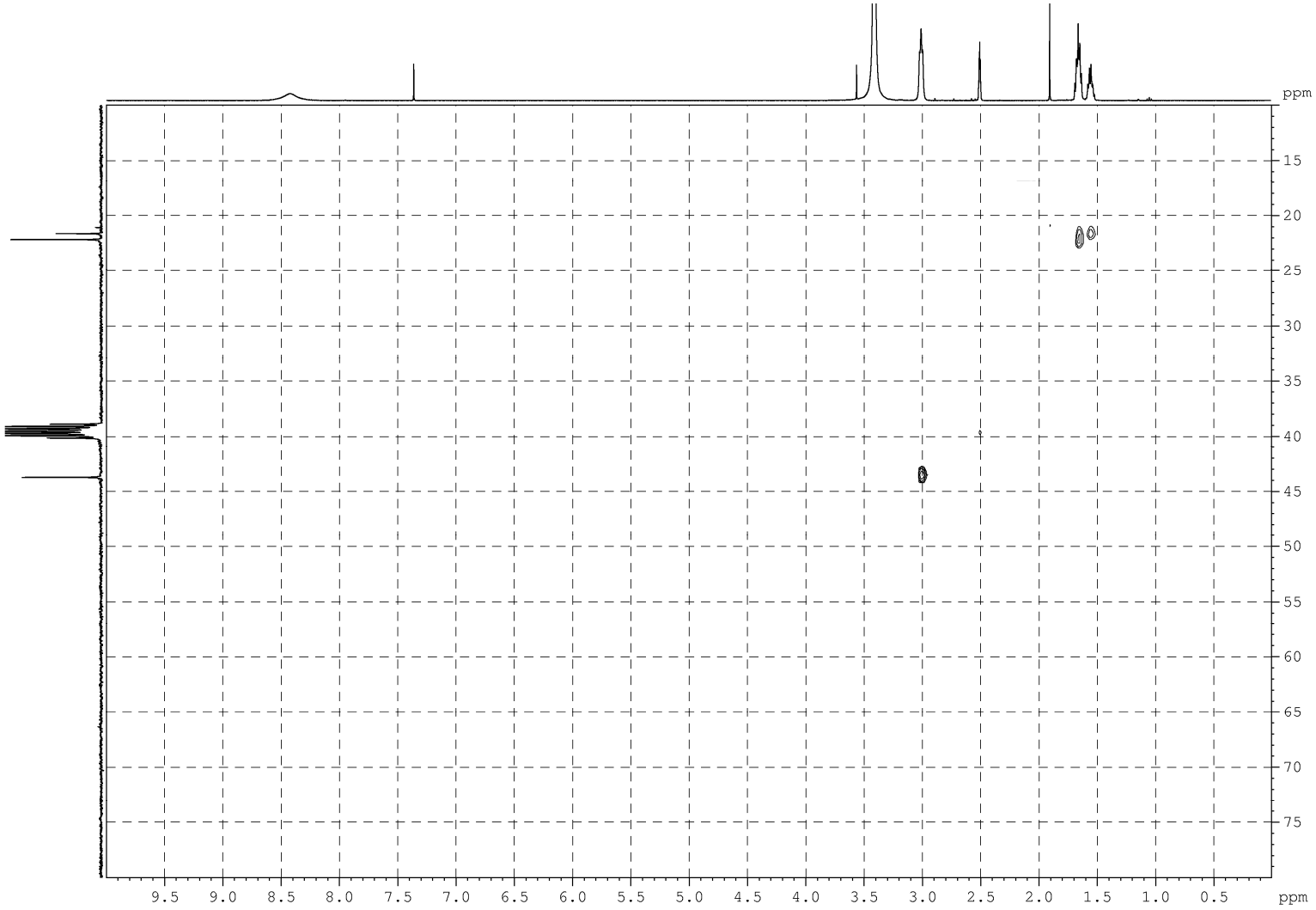

Figure S105. 2D ^{1}H-^{13}C HSQC NMR spectra of **6b** in DMSO at T = 303 K.

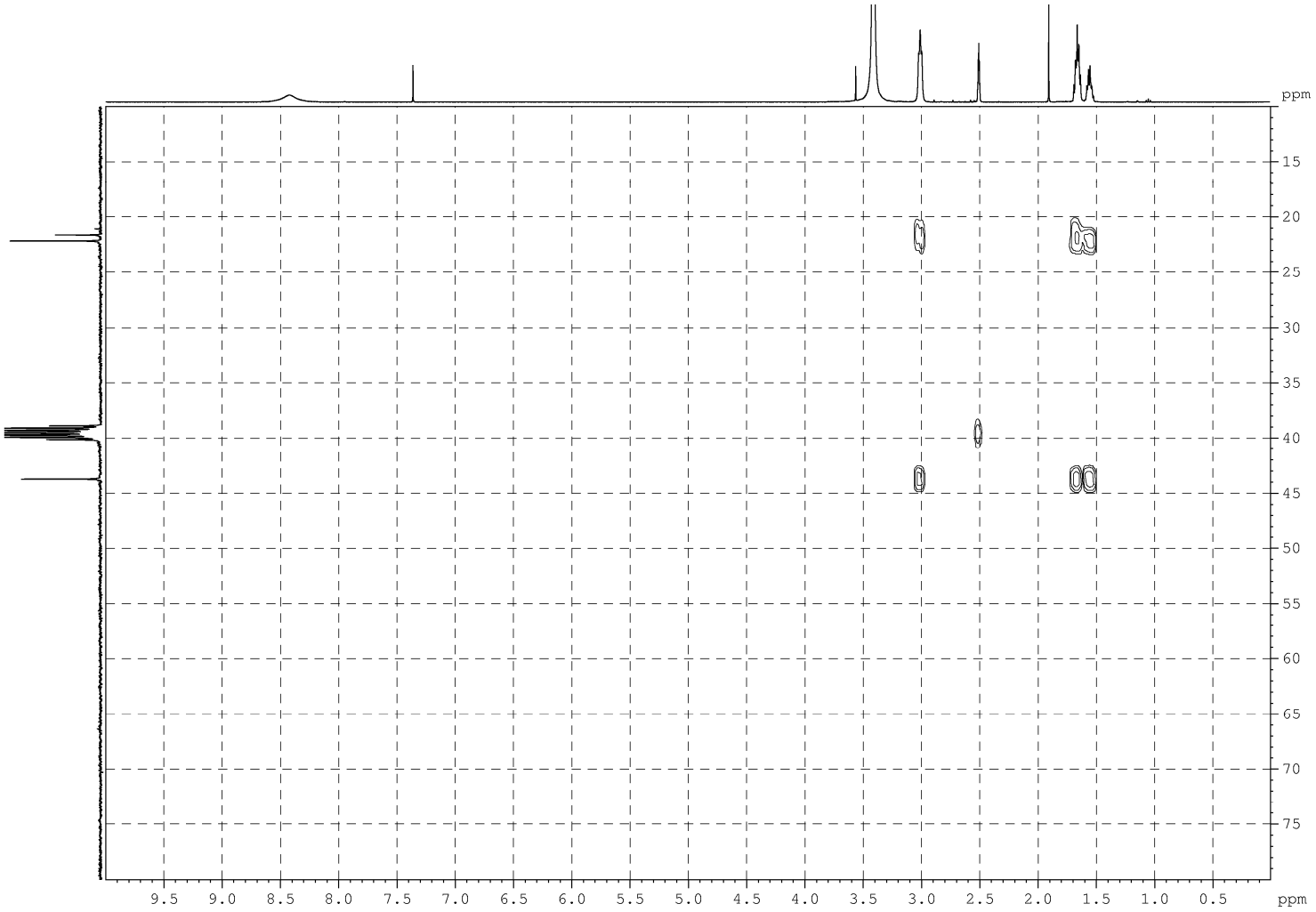

Figure S106. 2D ^{1}H-^{13}C HMBC NMR spectra of **6b** in DMSO at T = 303 K.

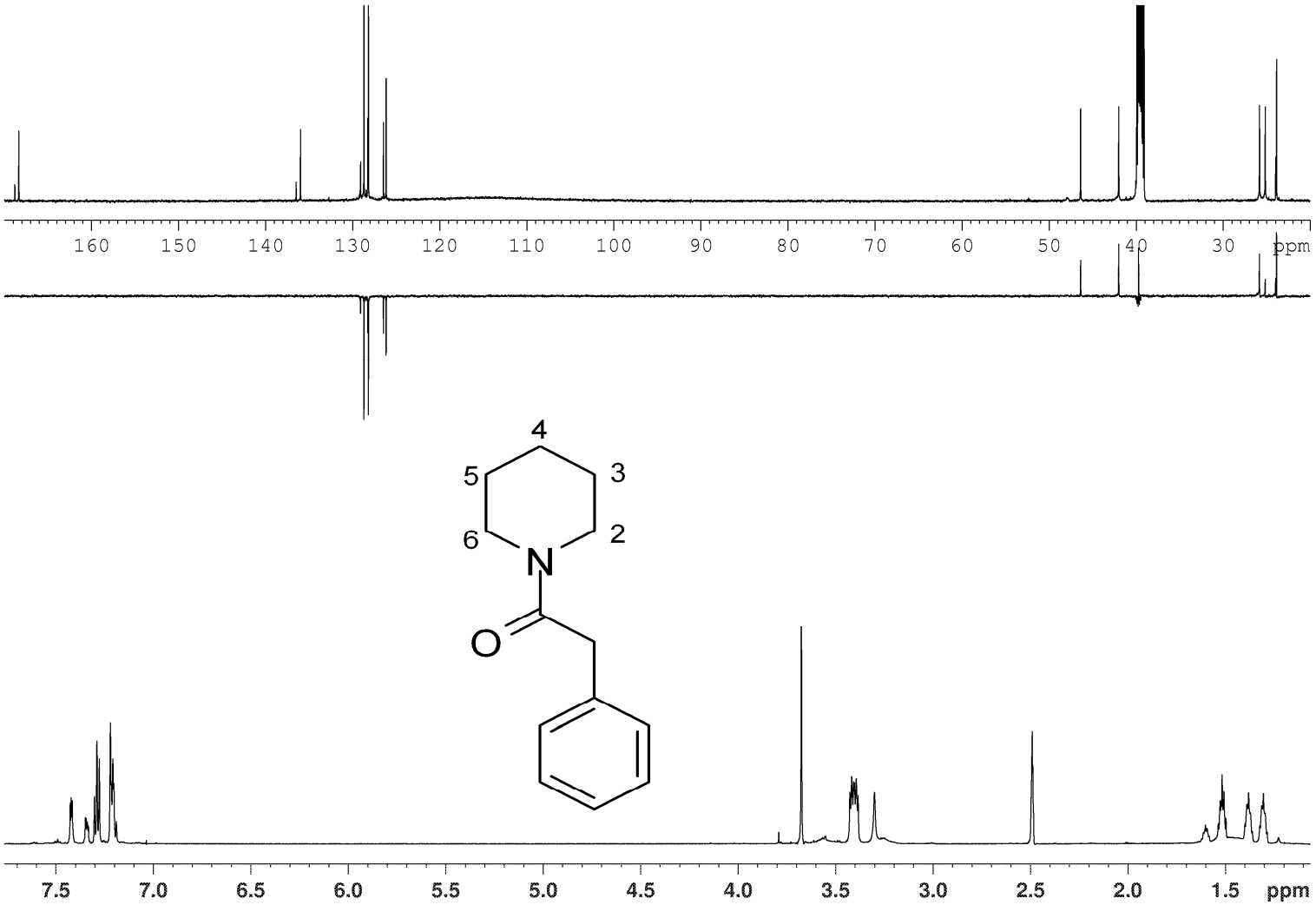

Figure S107. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **7a** in DMSO at T = 303 K.

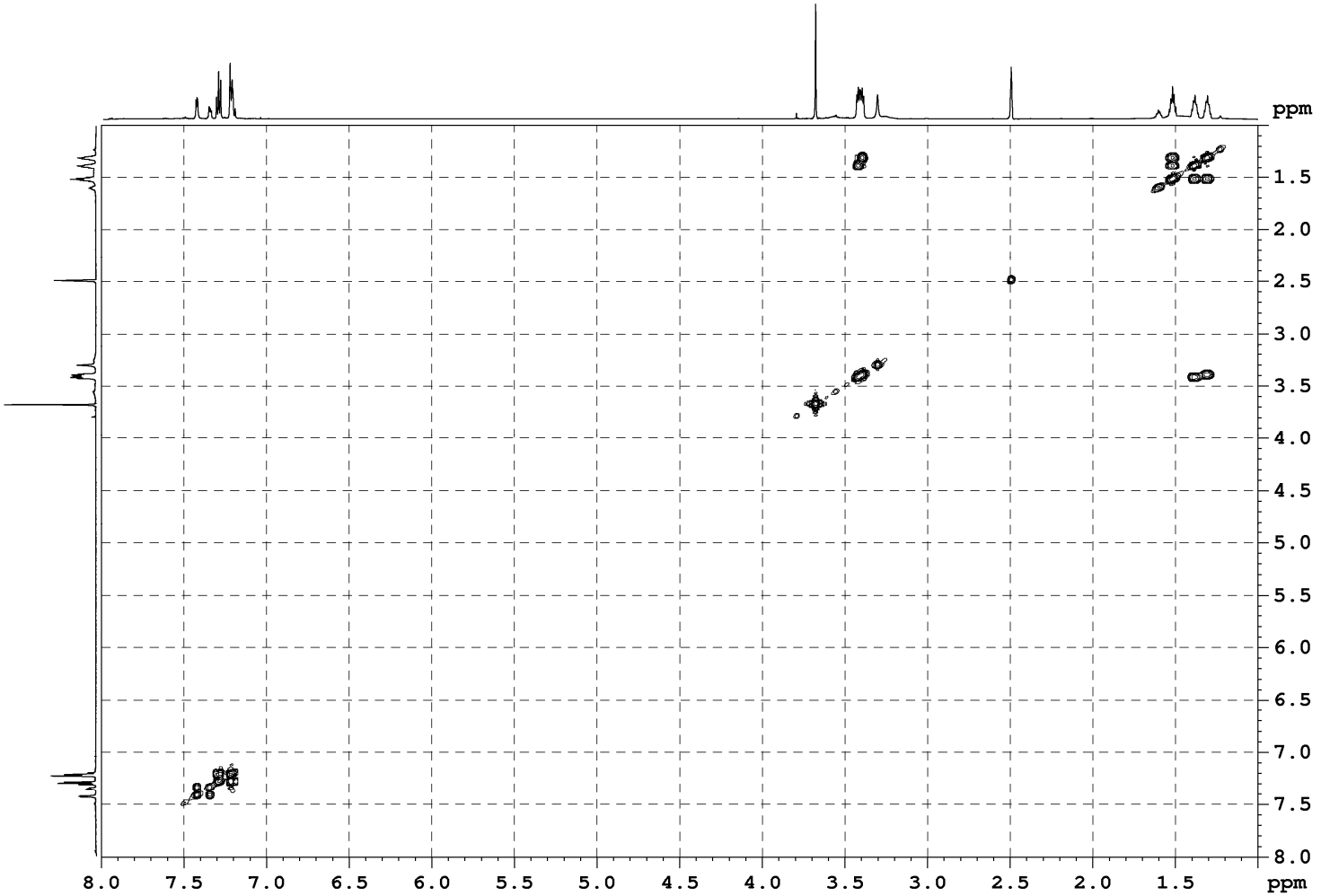

Figure S108. 2D ^{1}H-^{1}H COSY NMR spectra of **7a** in DMSO at T = 303 K.

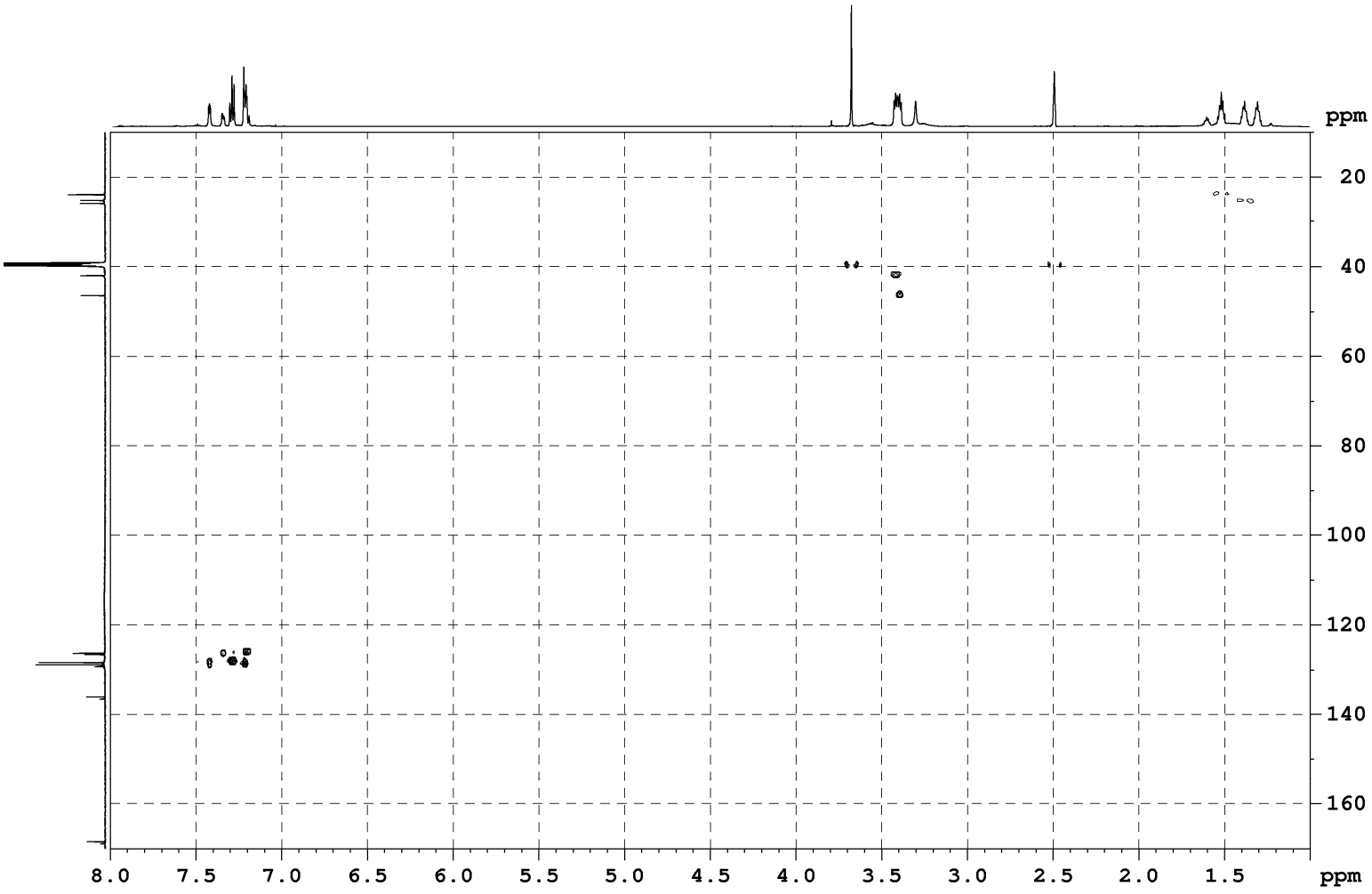

Figure S109. 2D ^{1}H-^{13}C HSQC NMR spectra of **7a** in DMSO at T = 303 K.

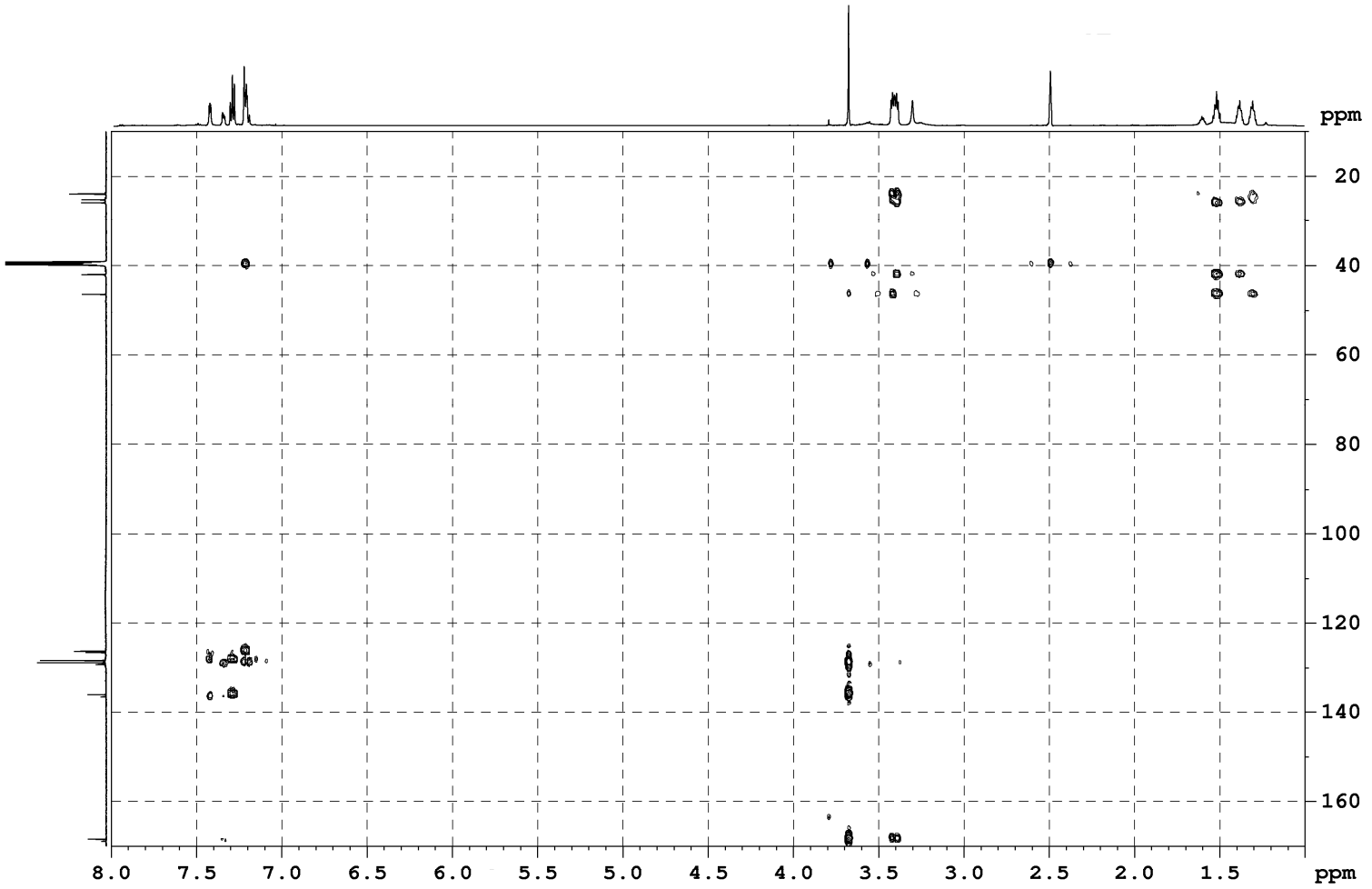

Figure S110. 2D ^{1}H-^{13}C HMBC NMR spectra of **7a** in DMSO at T = 303 K.

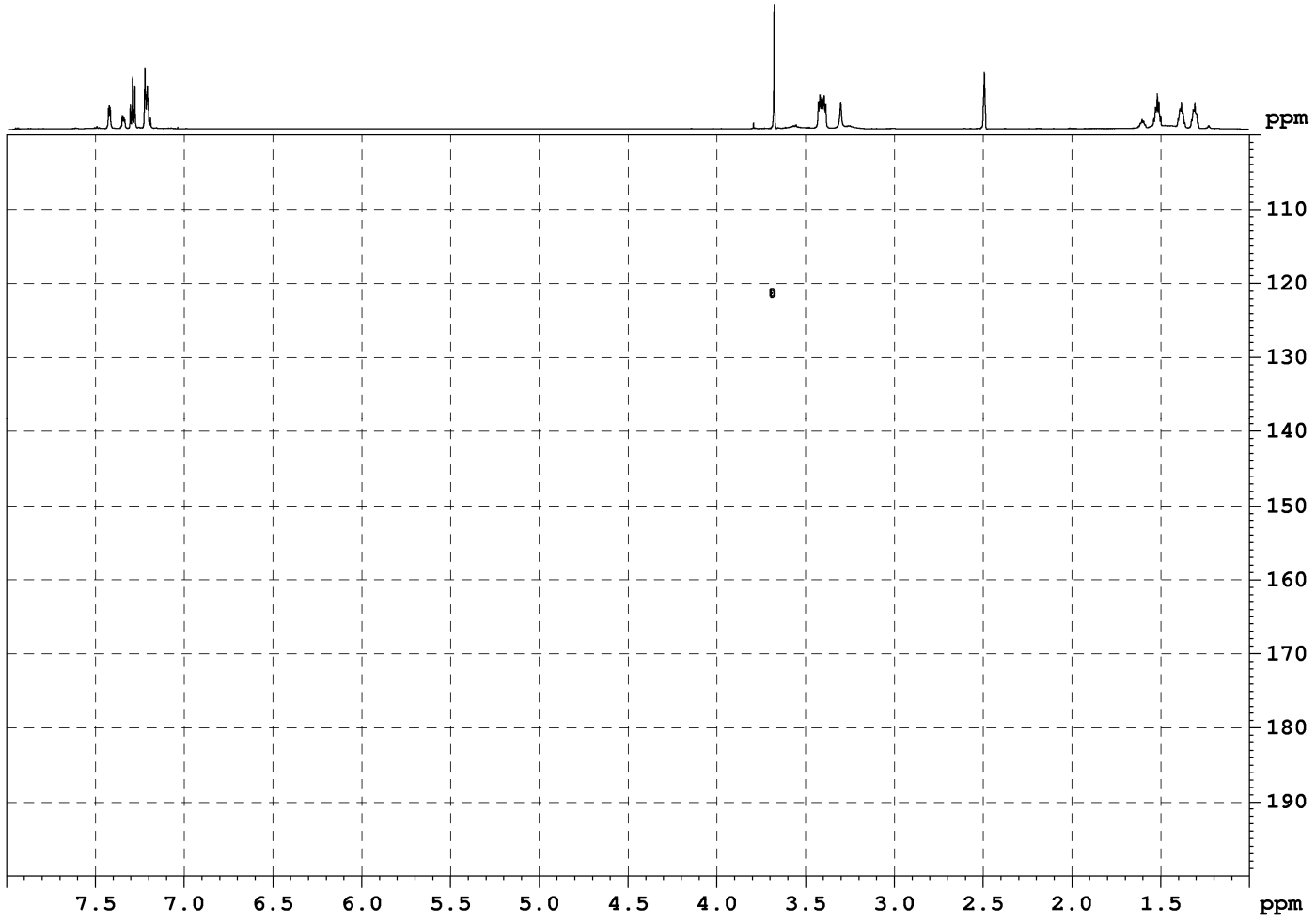

Figure S111. 2D ^{1}H-^{15}N HMBC NMR spectra of **7a** in DMSO at T = 303 K.

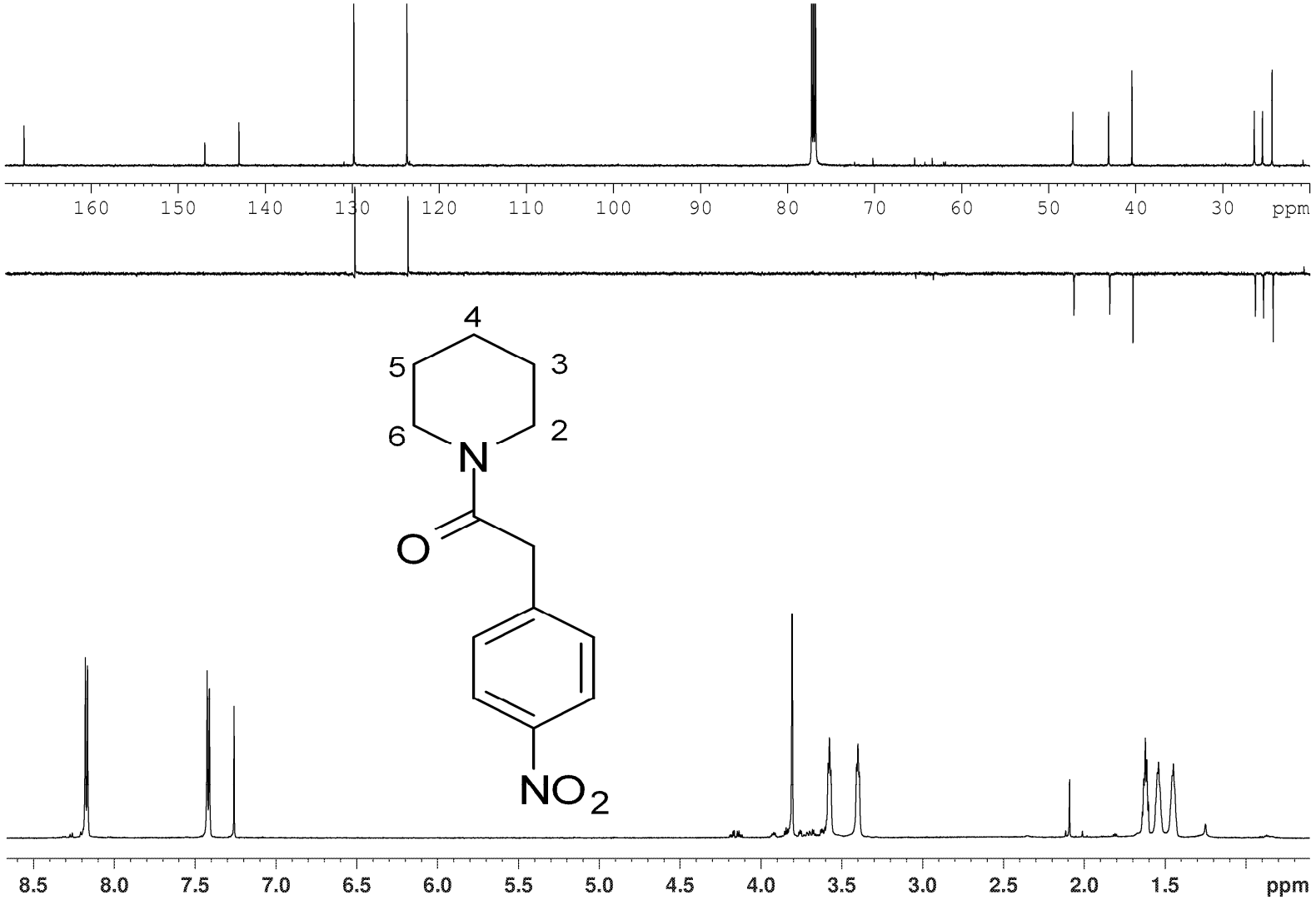

Figure S112. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **7g** in $CDCl_3$ at T = 303 K.

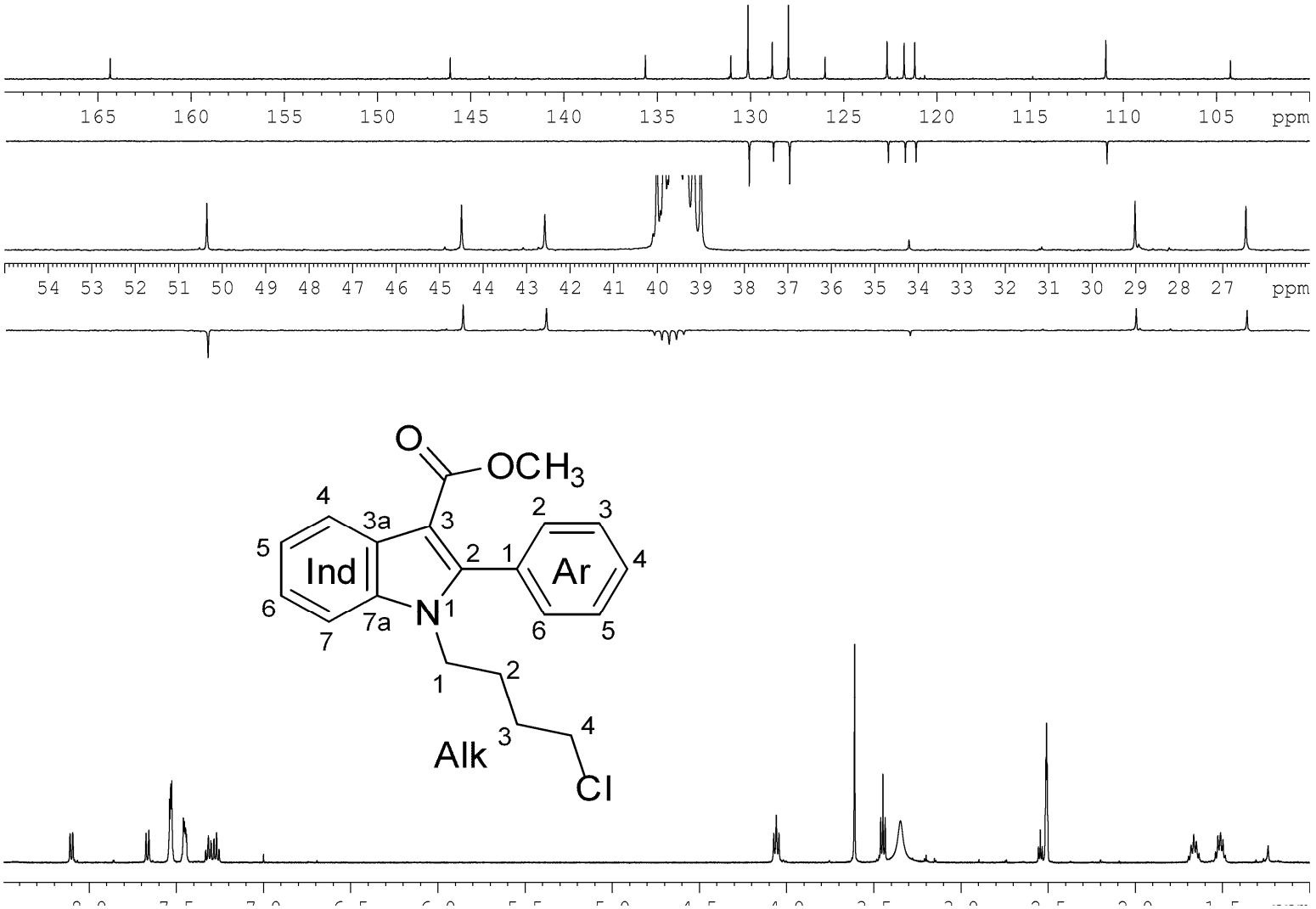

Figure S113. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **10a** in DMSO at T = 303 K.

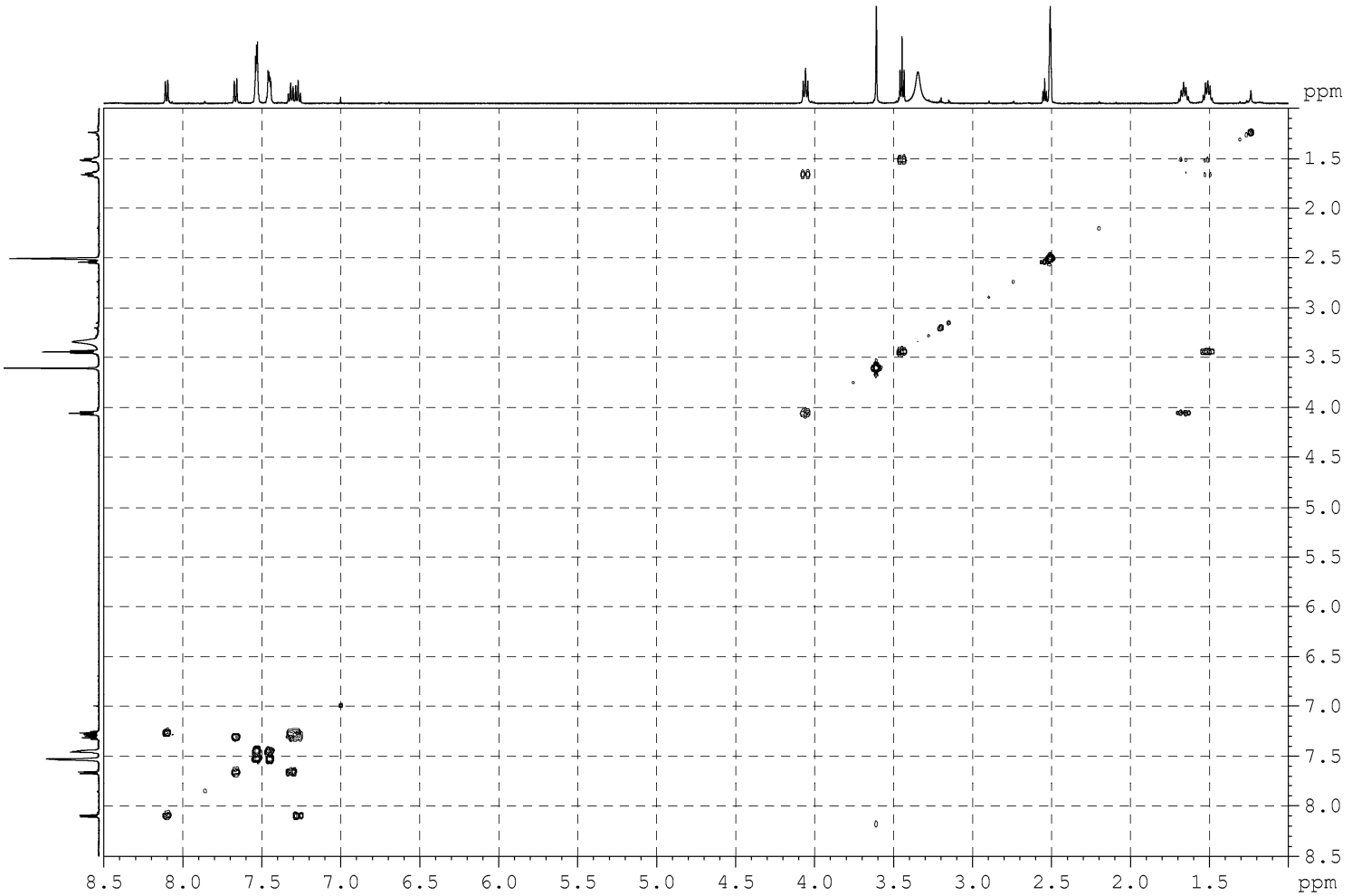

Figure S114. 2D ^{1}H-^{1}H COSY NMR spectra of **10a** in DMSO at T = 303 K.

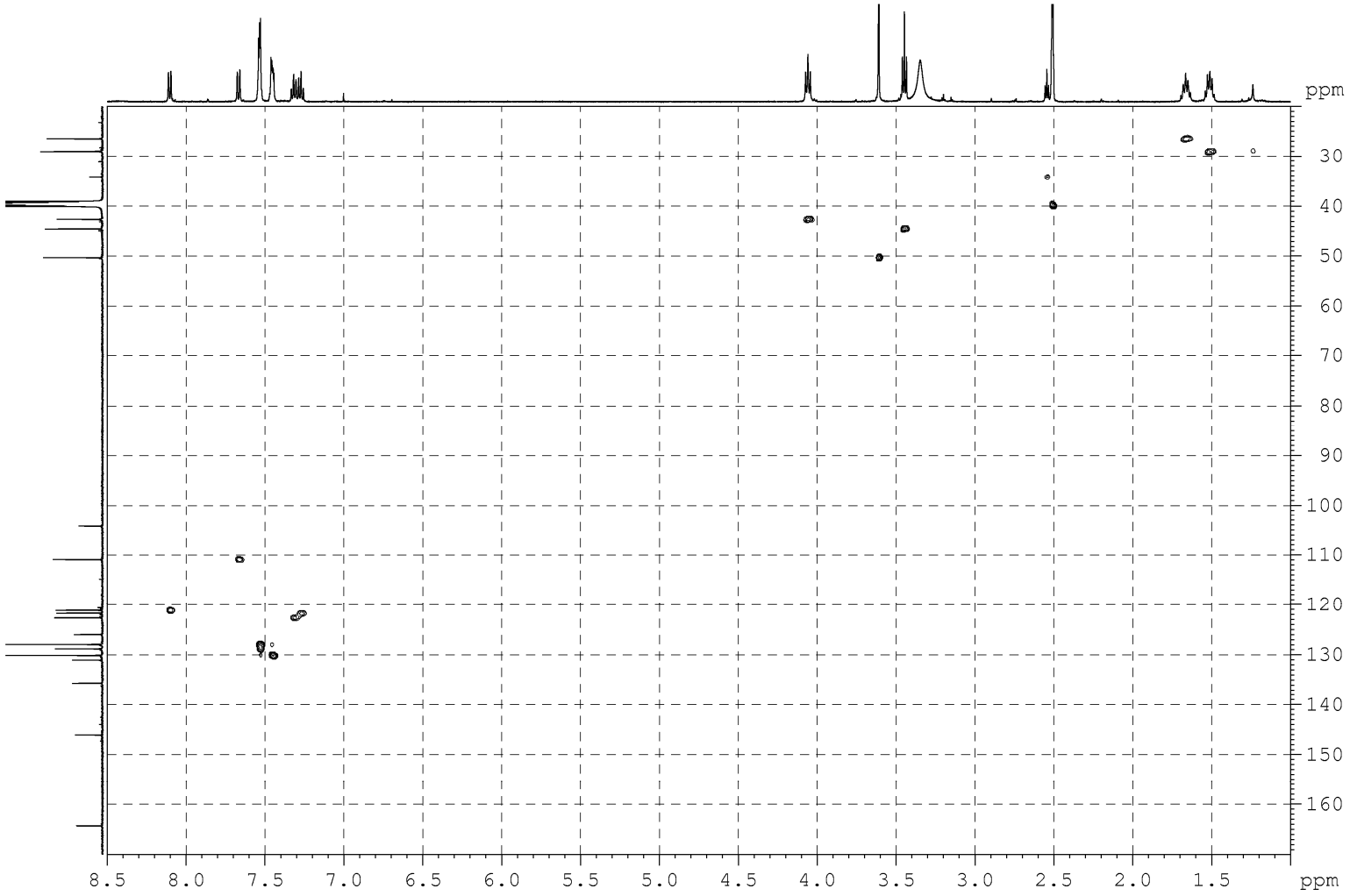

Figure S115. 2D ^{1}H-^{13}C HSQC NMR spectra of **10a** in DMSO at T = 303 K.

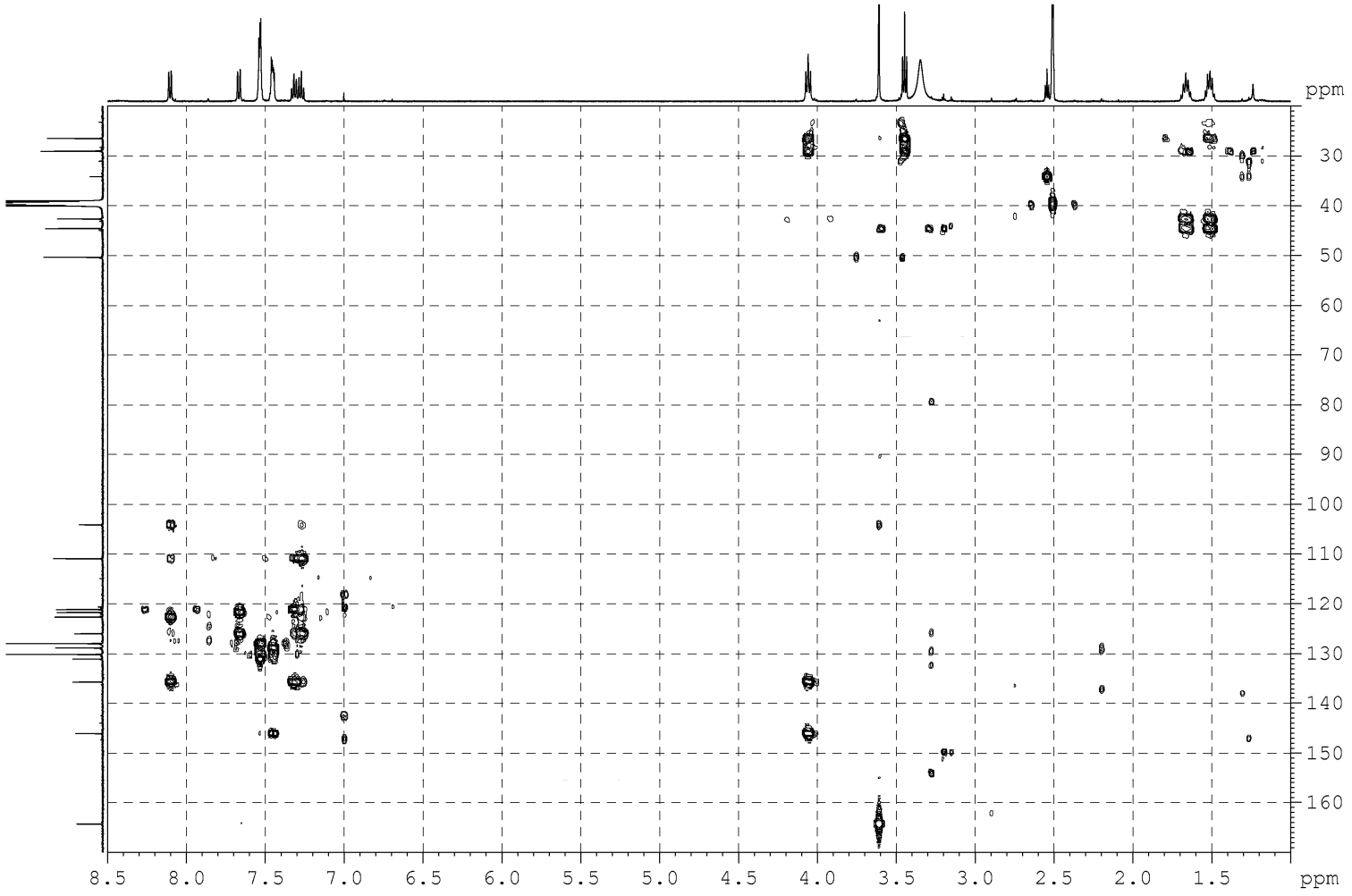

Figure S116. 2D ^{1}H-^{13}C HMBC NMR spectra of **10a** in DMSO at T = 303 K.

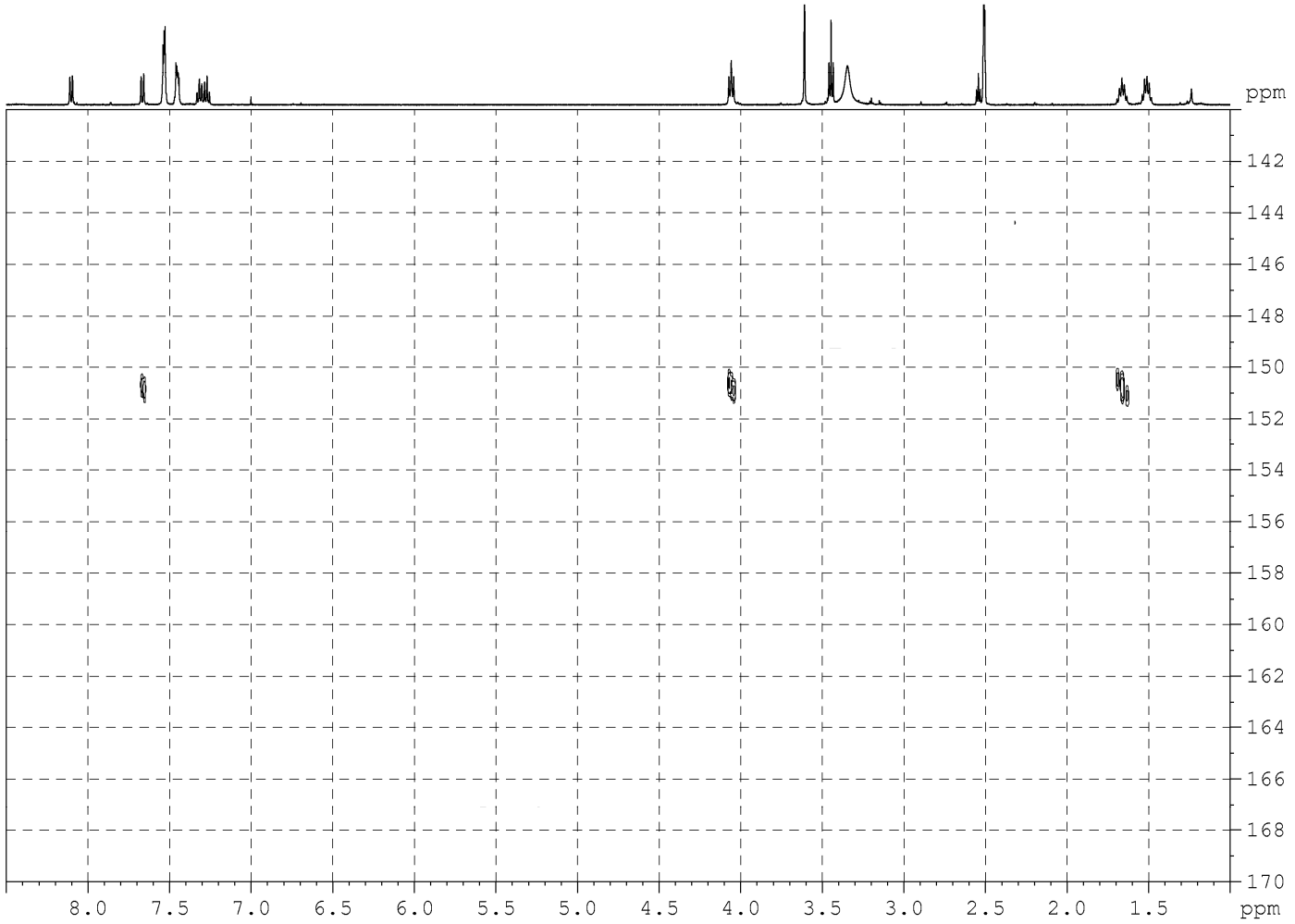

Figure S117. 2D ^{1}H-^{15}N HMBC NMR spectra of **10a** in DMSO at T = 303 K.

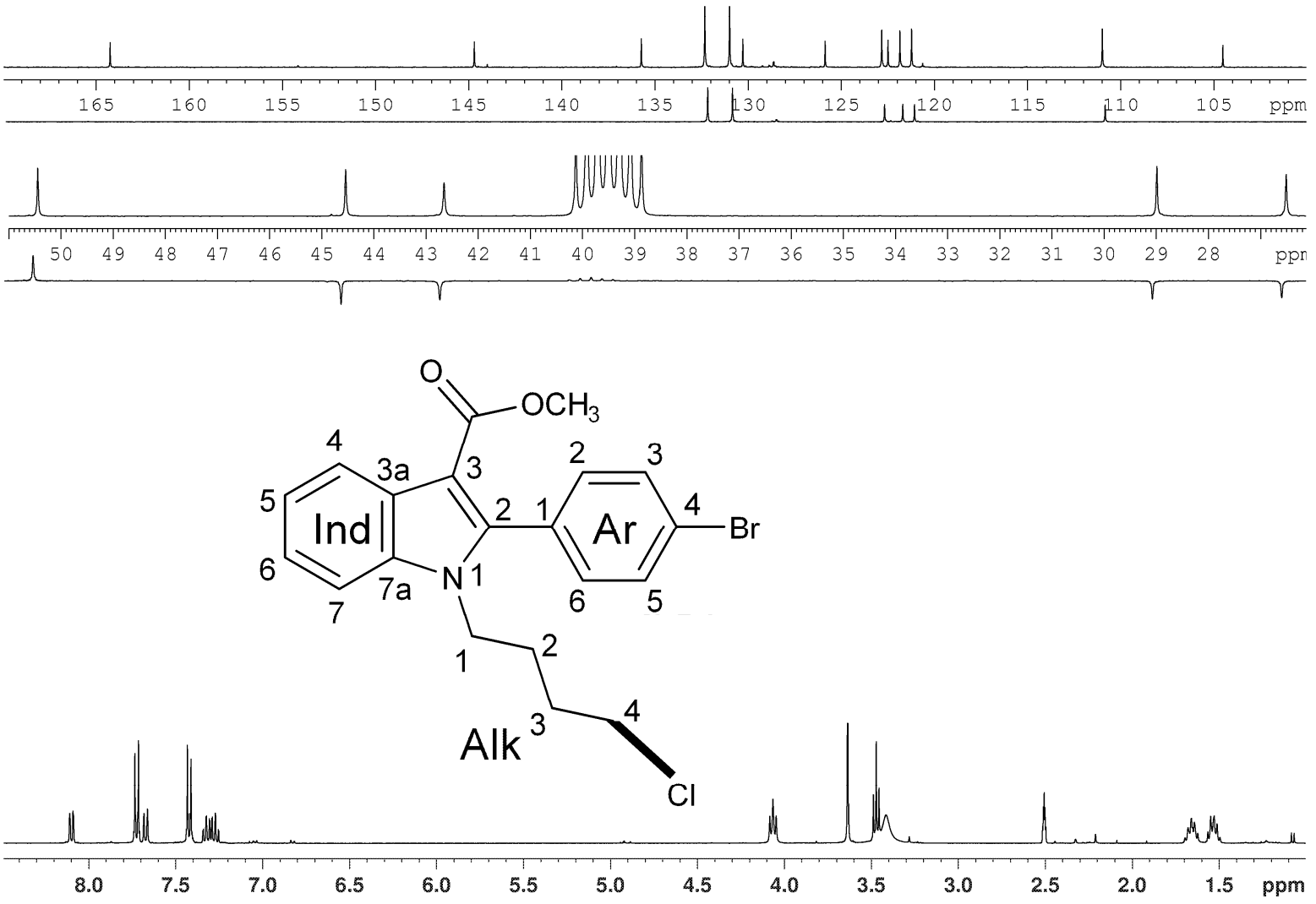

Figure S118. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **10c** in DMSO at T = 303 K.

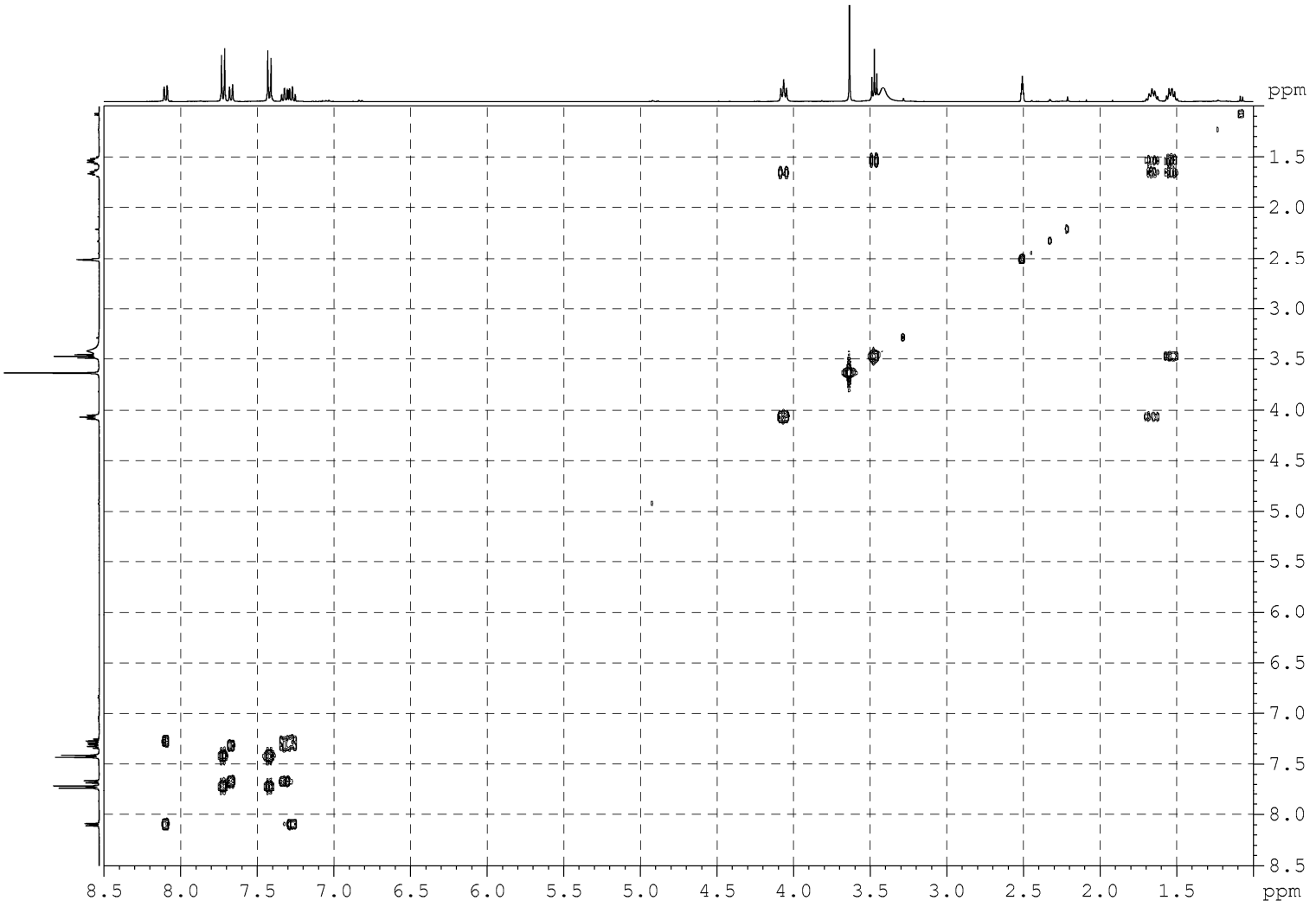

Figure S119. 2D ^{1}H-^{1}H COSY NMR spectra of **10c** in DMSO at T = 303 K.

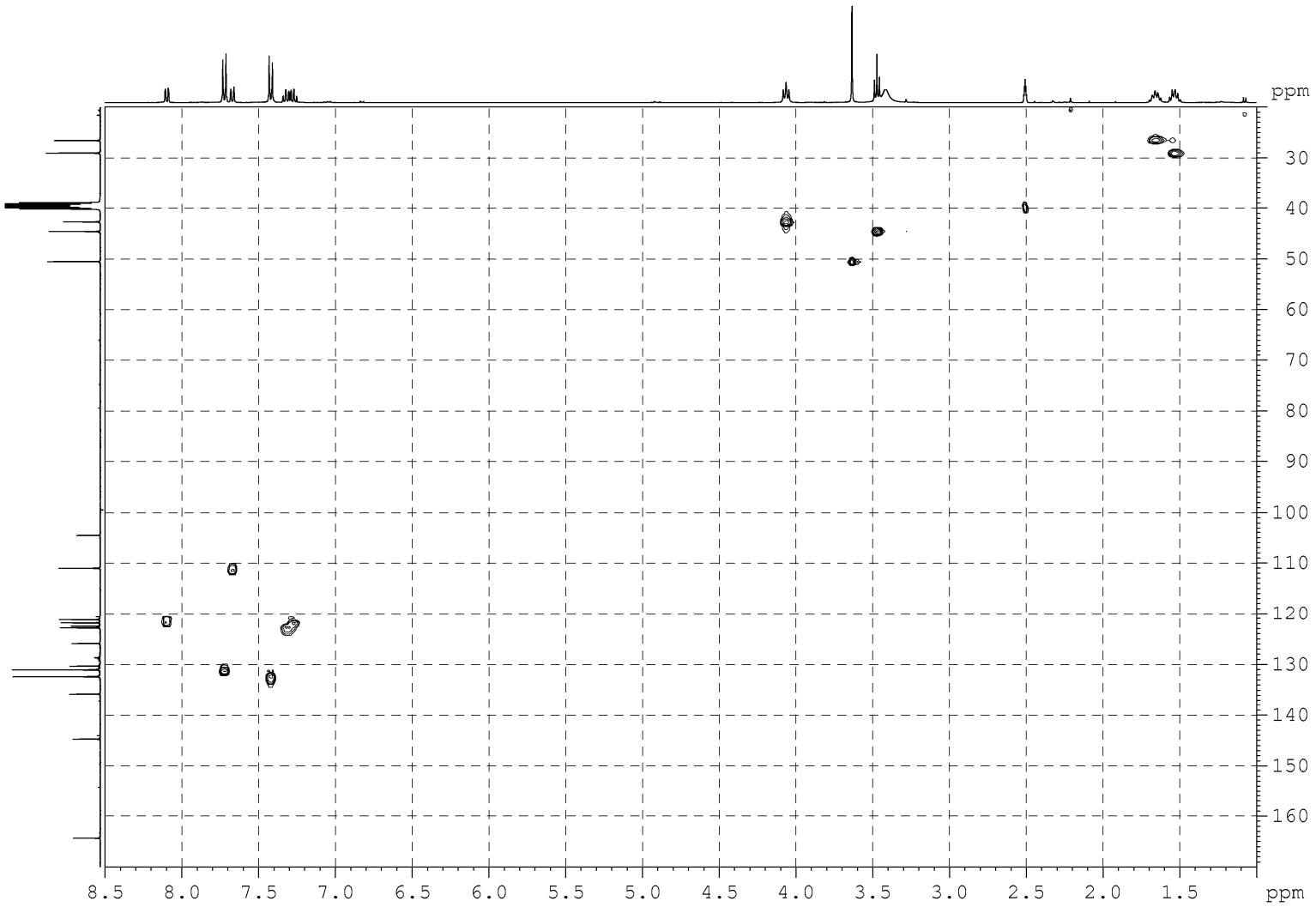

Figure S120. 2D ^{1}H-^{13}C HSQC NMR spectra of **10c** in DMSO at T = 303 K.

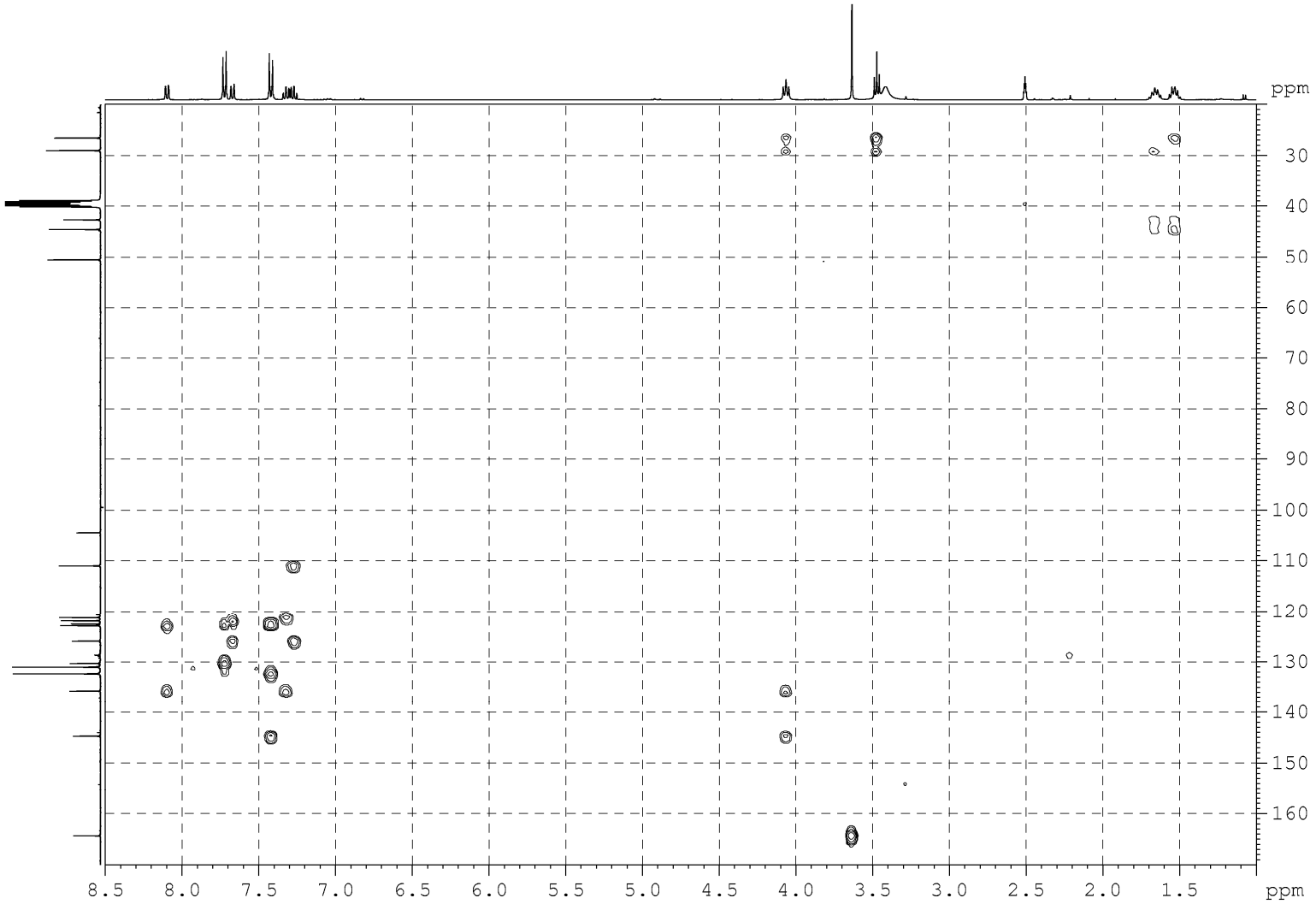

Figure S121. 2D ^{1}H-^{13}C HMBC NMR spectra of **10c** in DMSO at T = 303 K.

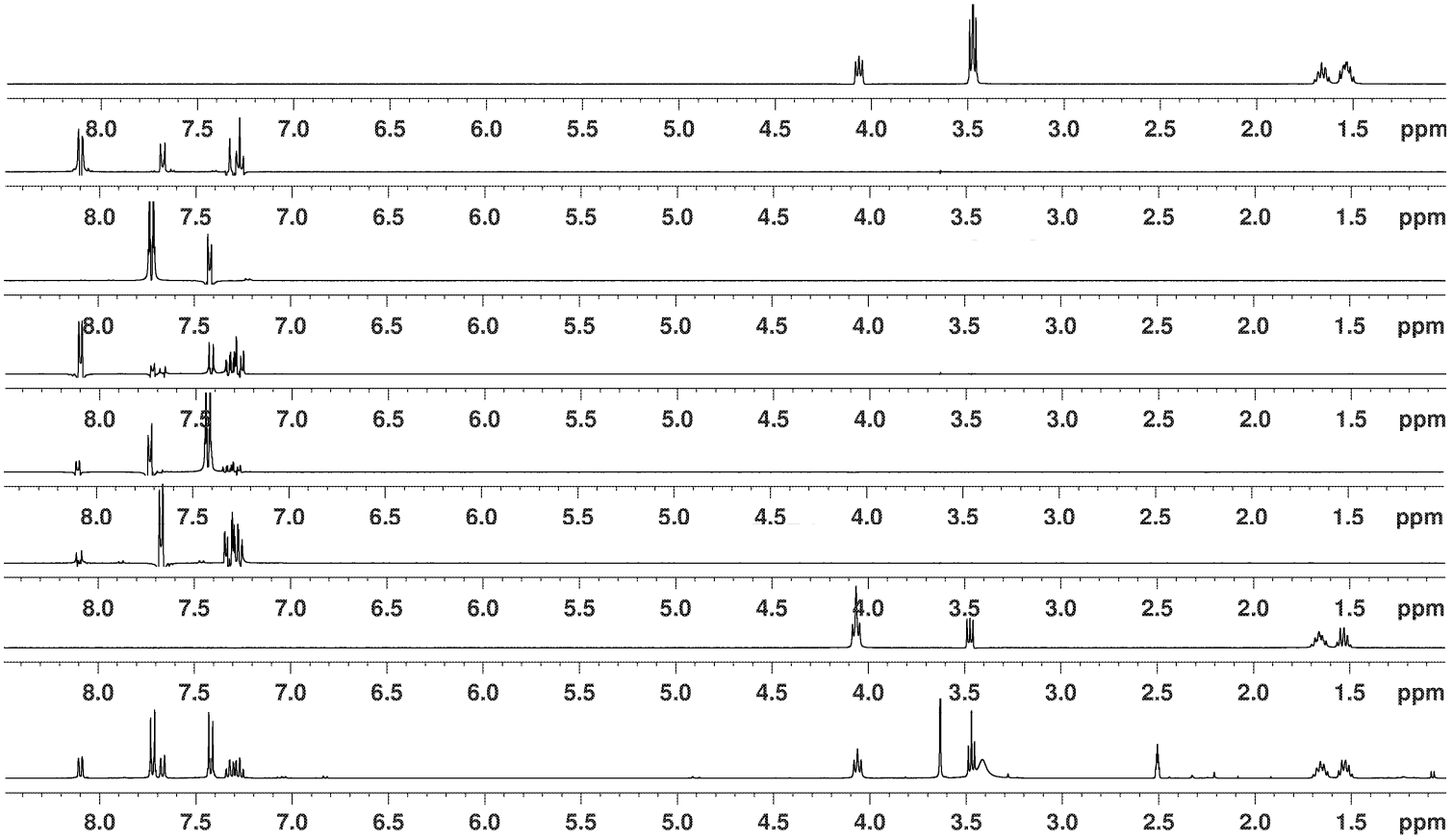

Figure S122. 1D ^{1}H and ^{1}H TOCSY NMR spectra of **10c** in DMSO at T = 303 K.

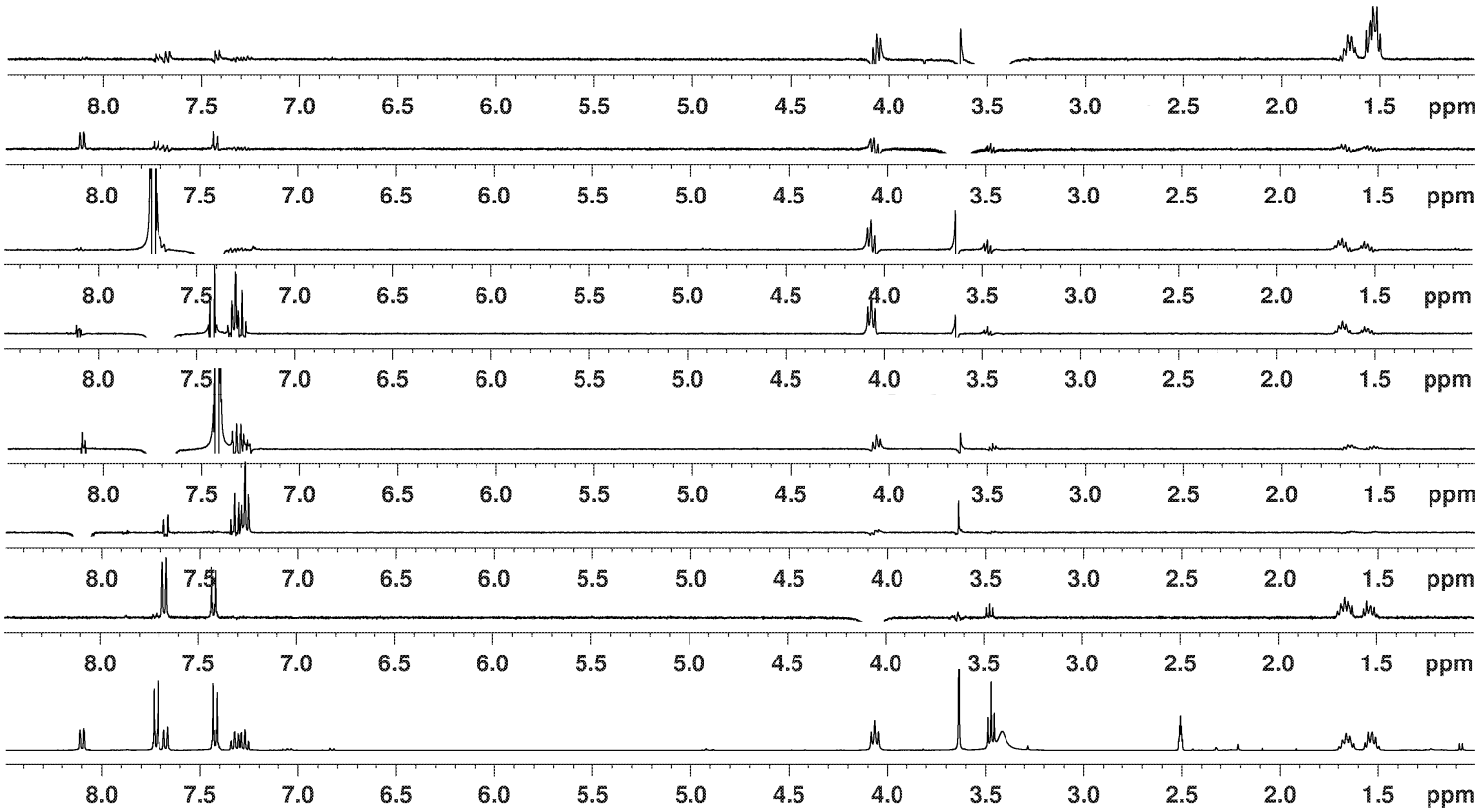

Figure S123. 1D ^{1}H and ^{1}H DPFGROE NMR spectra of **10c** in DMSO at T = 303 K.

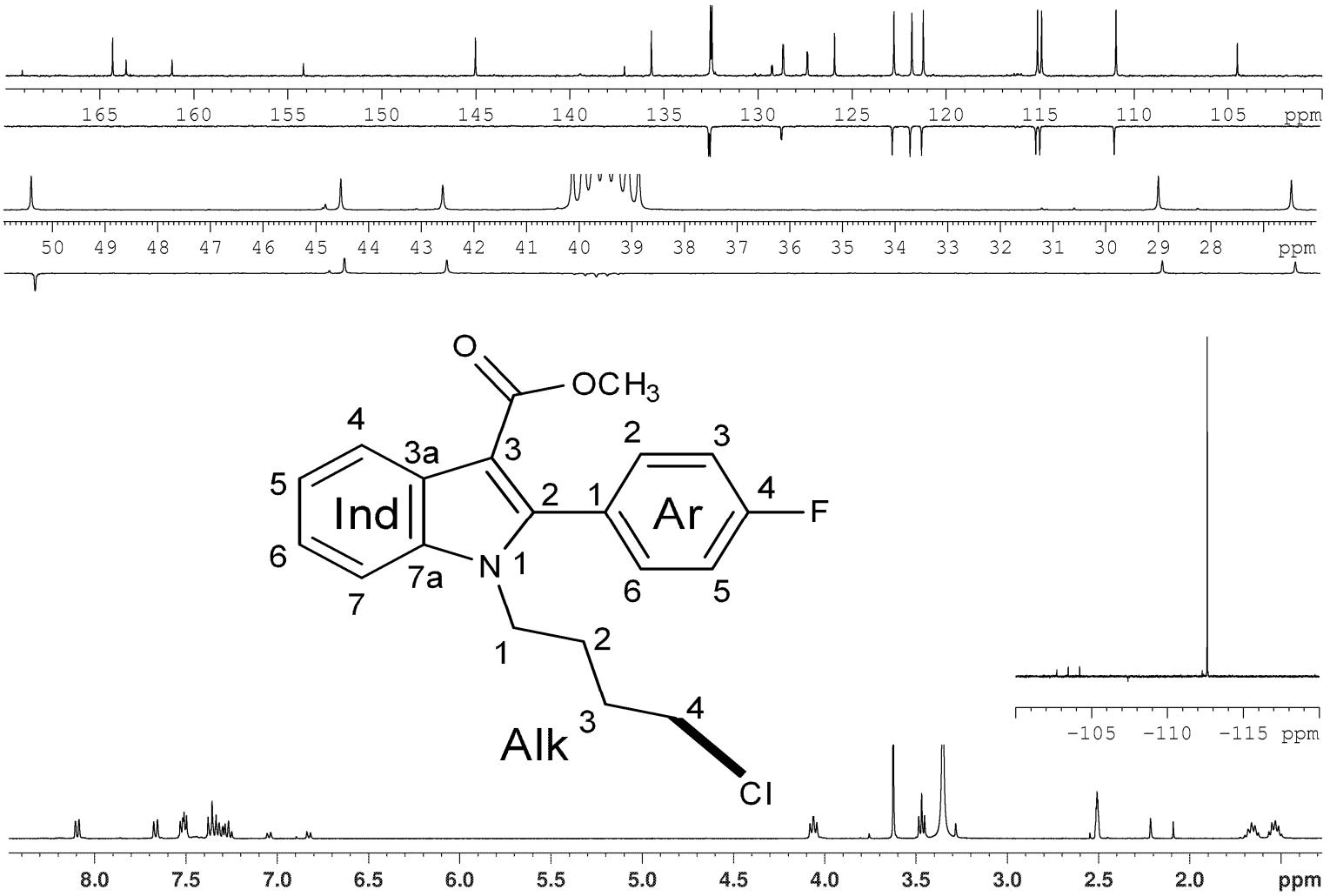

Figure S124. 1D ^{1}H, ^{13}C DEPT, $^{13}C\{^{1}H\}$ and $^{19}F\{^{1}H\}$ NMR spectra of **10d** in DMSO at T = 303 K.

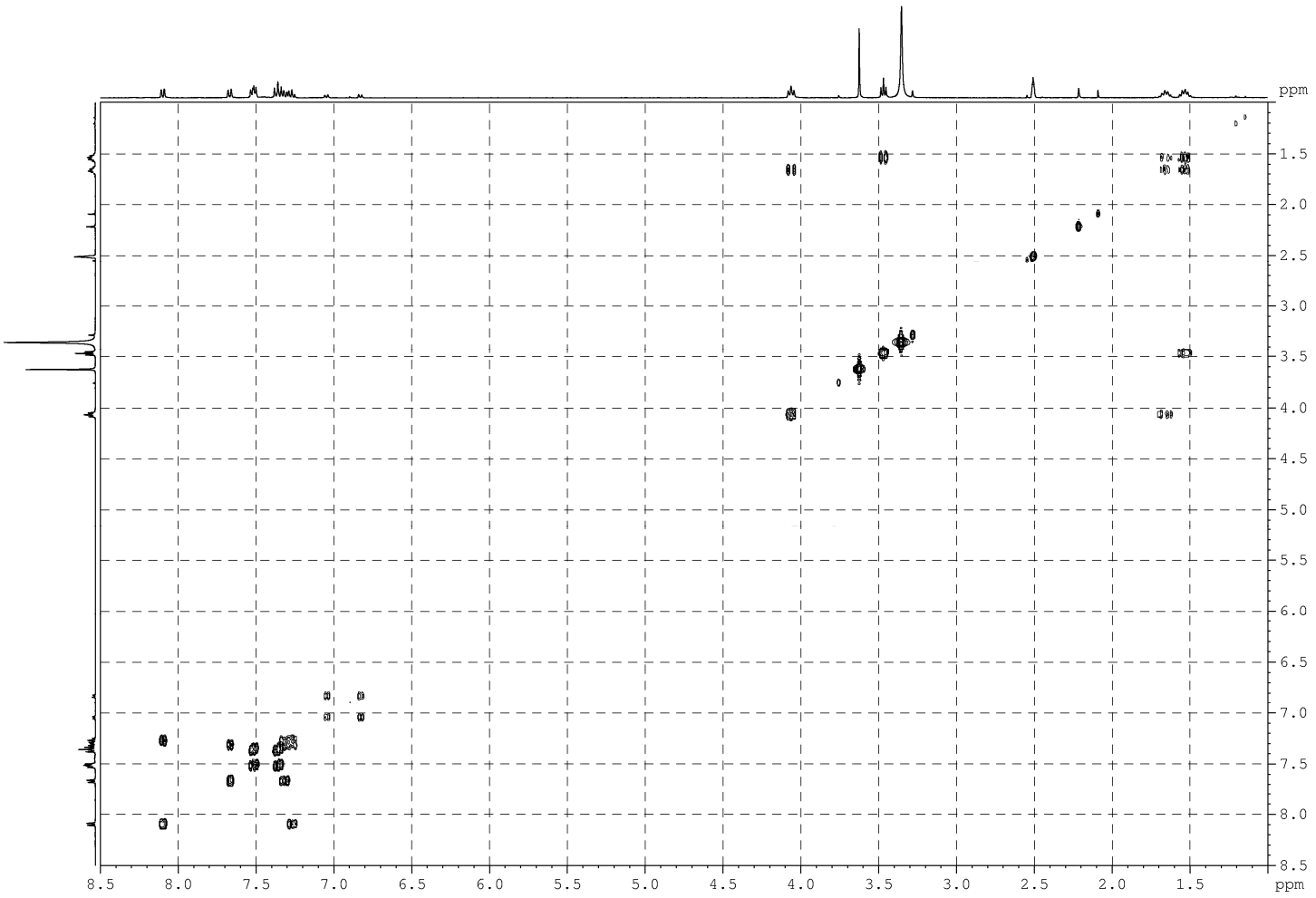

Figure S125. 2D ^{1}H-^{1}H COSY NMR spectra of **10d** in DMSO at T = 303 K.

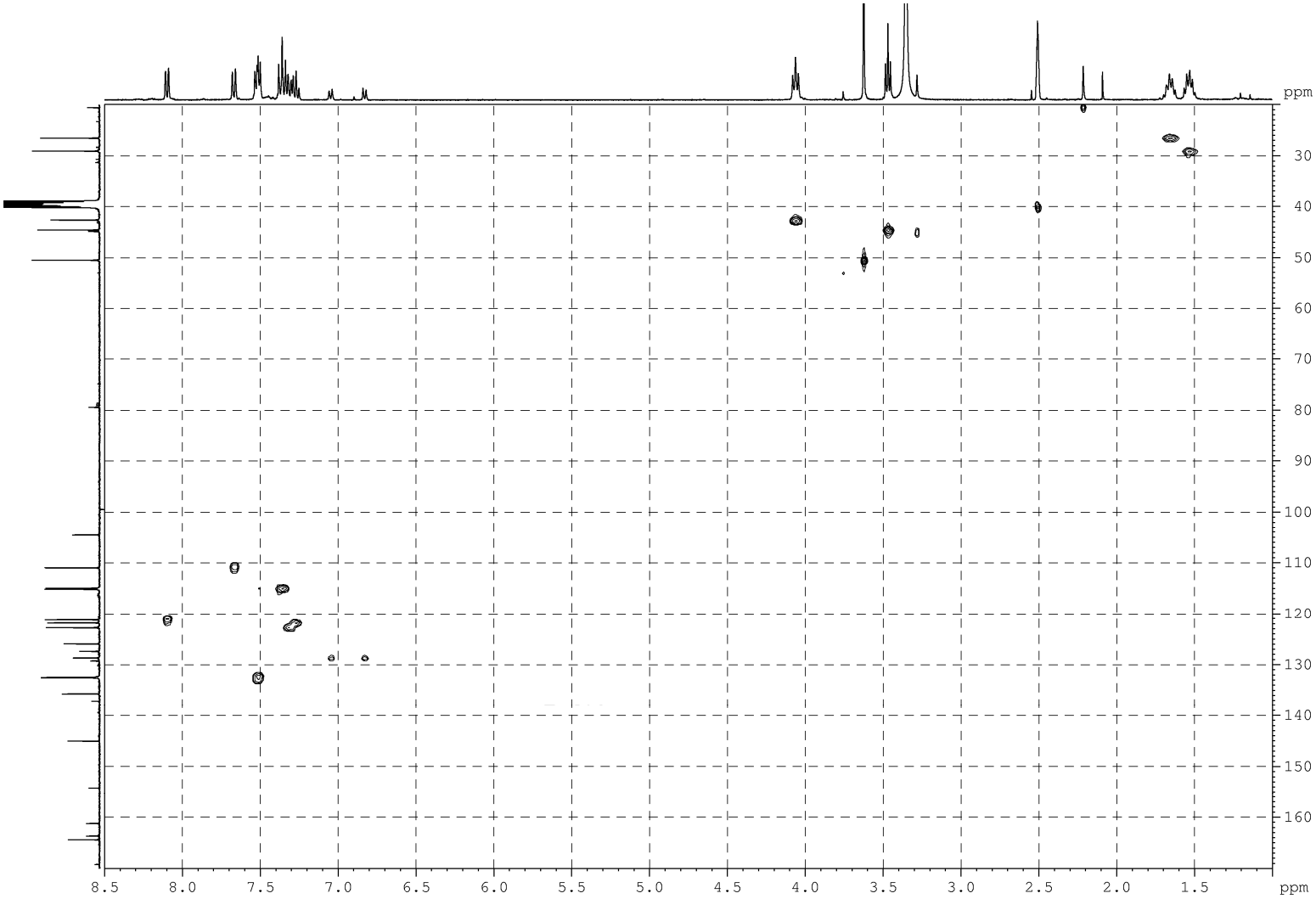

Figure S126. 2D ^{1}H-^{13}C HSQC NMR spectra of **10d** in DMSO at T = 303 K.

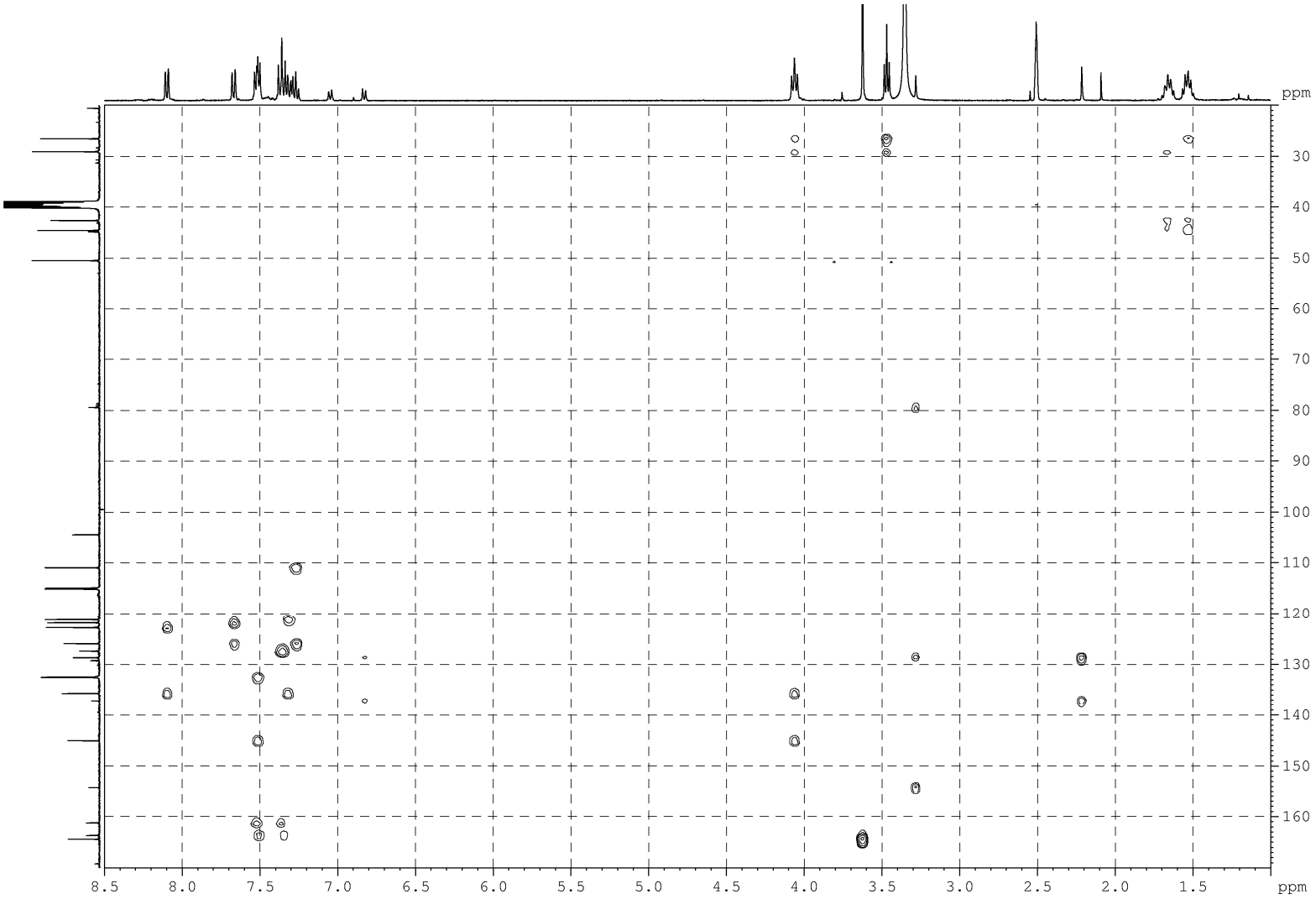

Figure S127. 2D ^{1}H-^{13}C HMBC NMR spectra of **10d** in DMSO at T = 303 K.

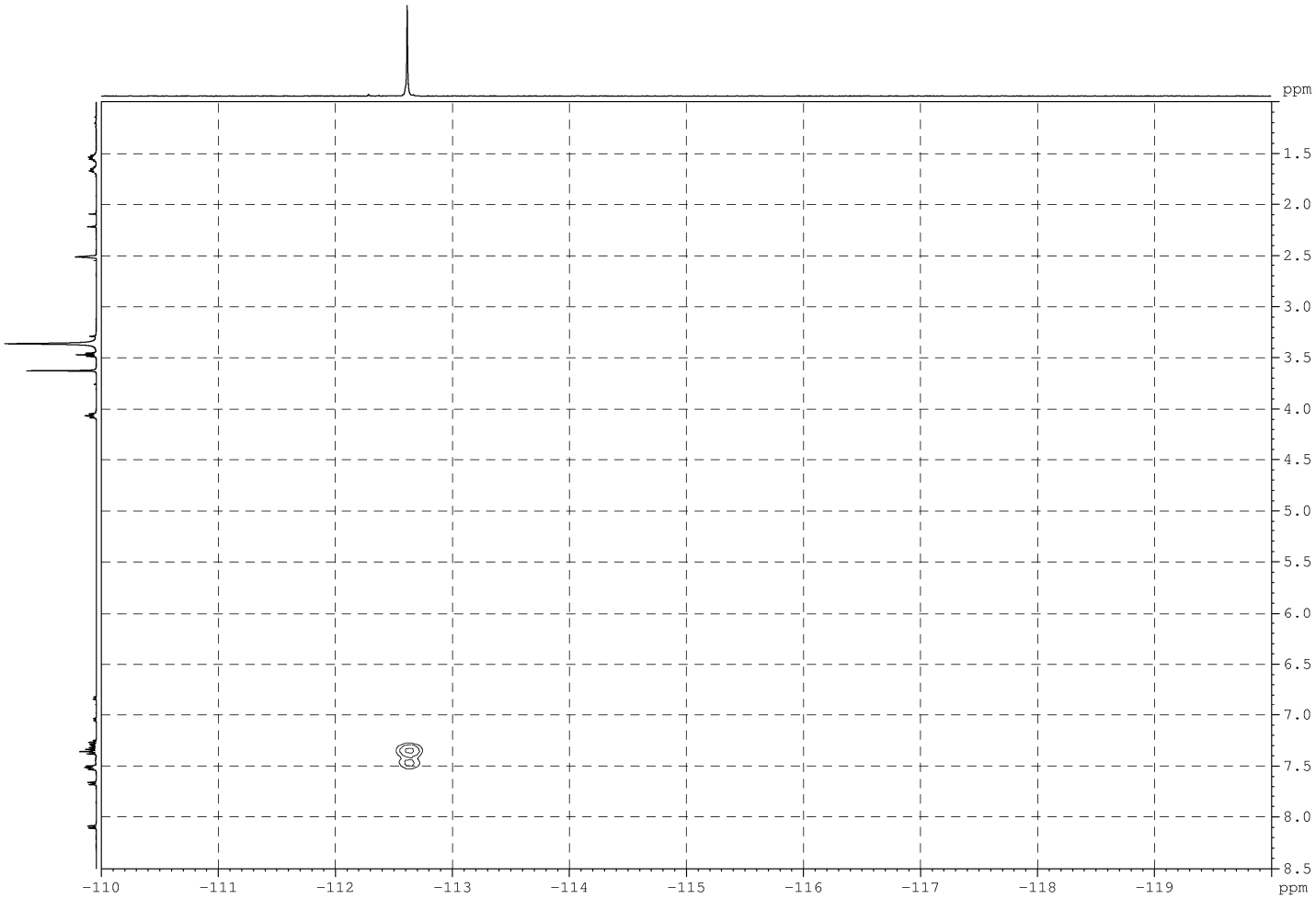

Figure S128. 2D ^{1}H-^{19}F HMBC NMR spectra of **10d** in DMSO at T = 303 K.

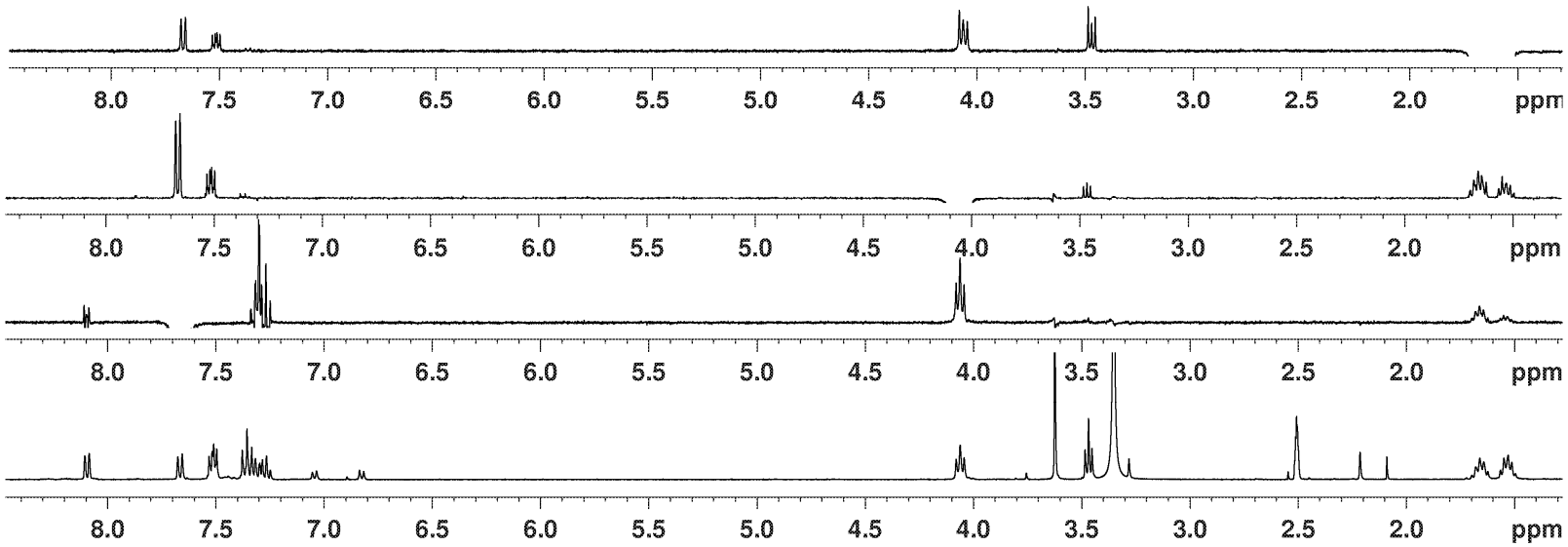

Figure S129. 1D ^{1}H and ^{1}H DPFGROE NMR spectra of **10d** in DMSO at T = 303 K.

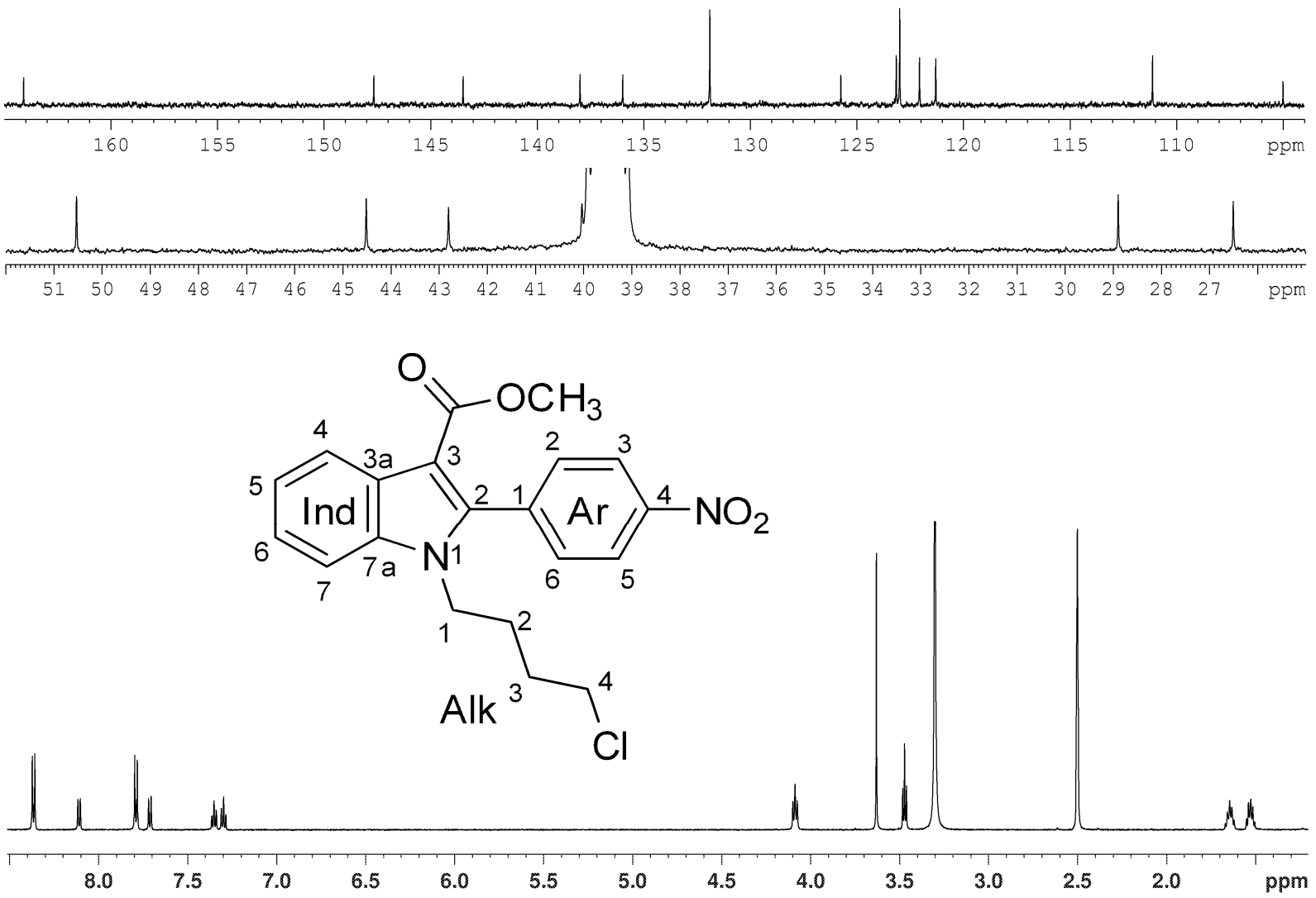

Figure S130. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **10g** in DMSO at T = 303 K.

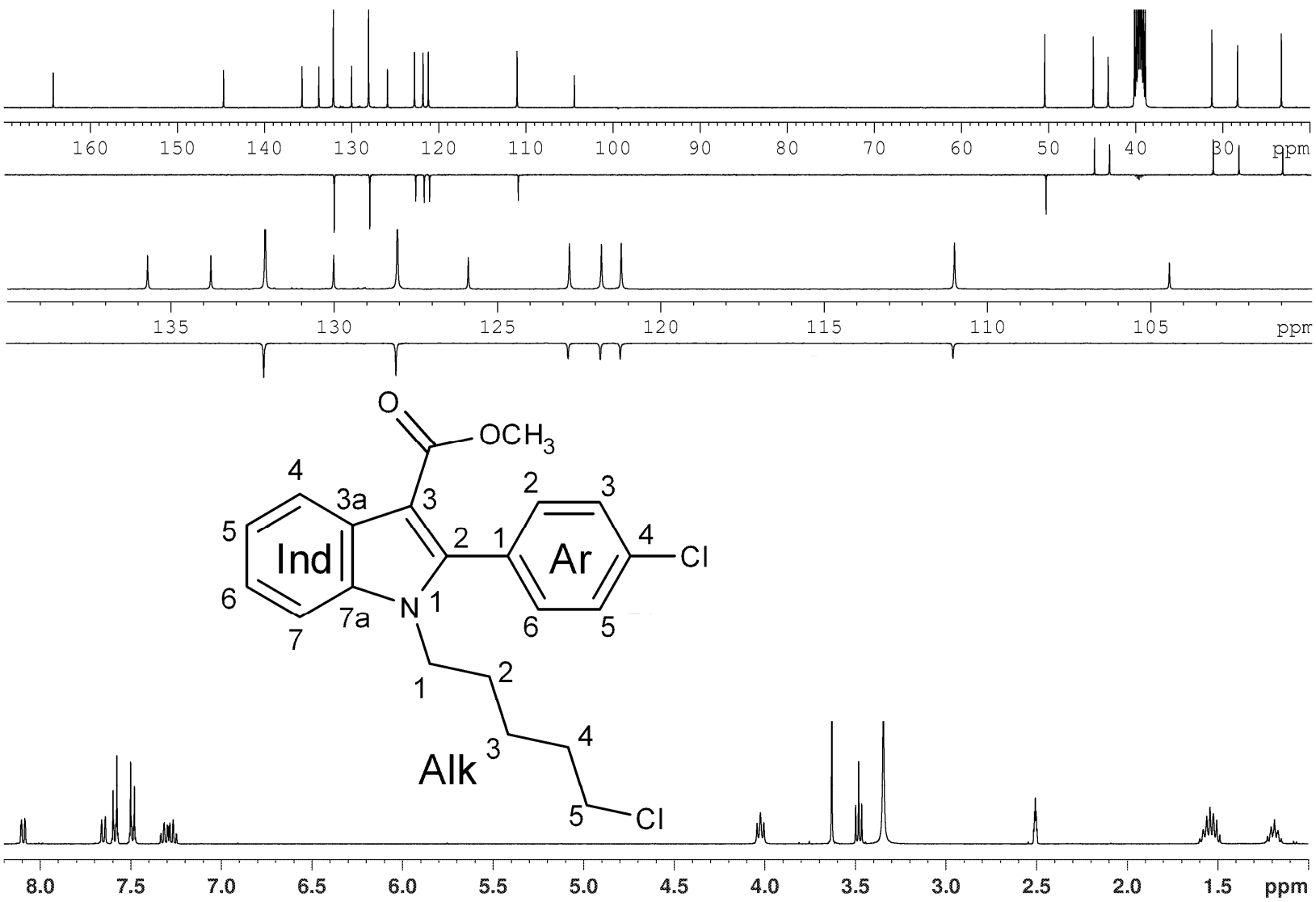

Figure S131. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **11b** in DMSO at T = 303 K.

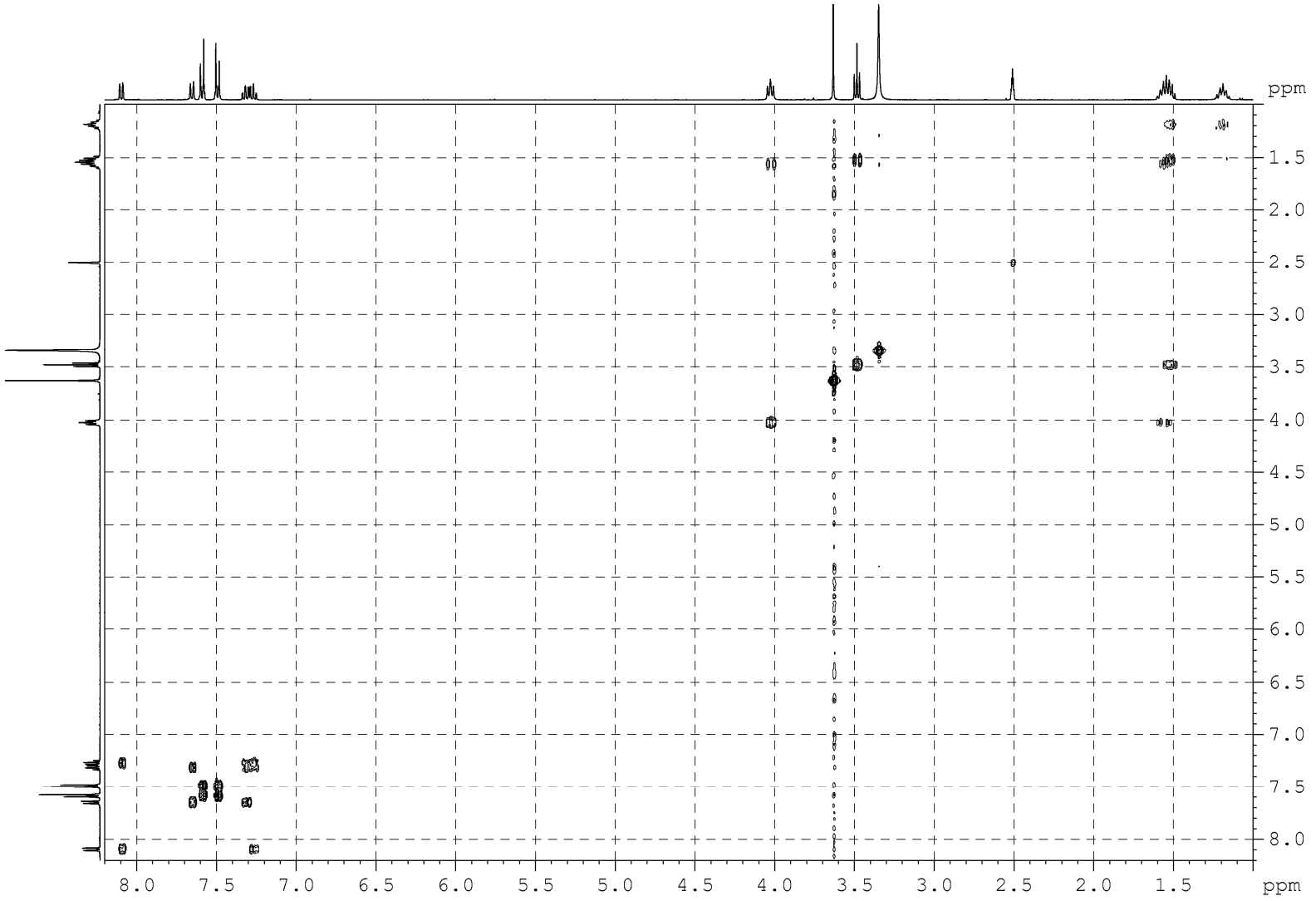

Figure S132. 2D ^{1}H-^{1}H COSY NMR spectra of **11b** in DMSO at T = 303 K.

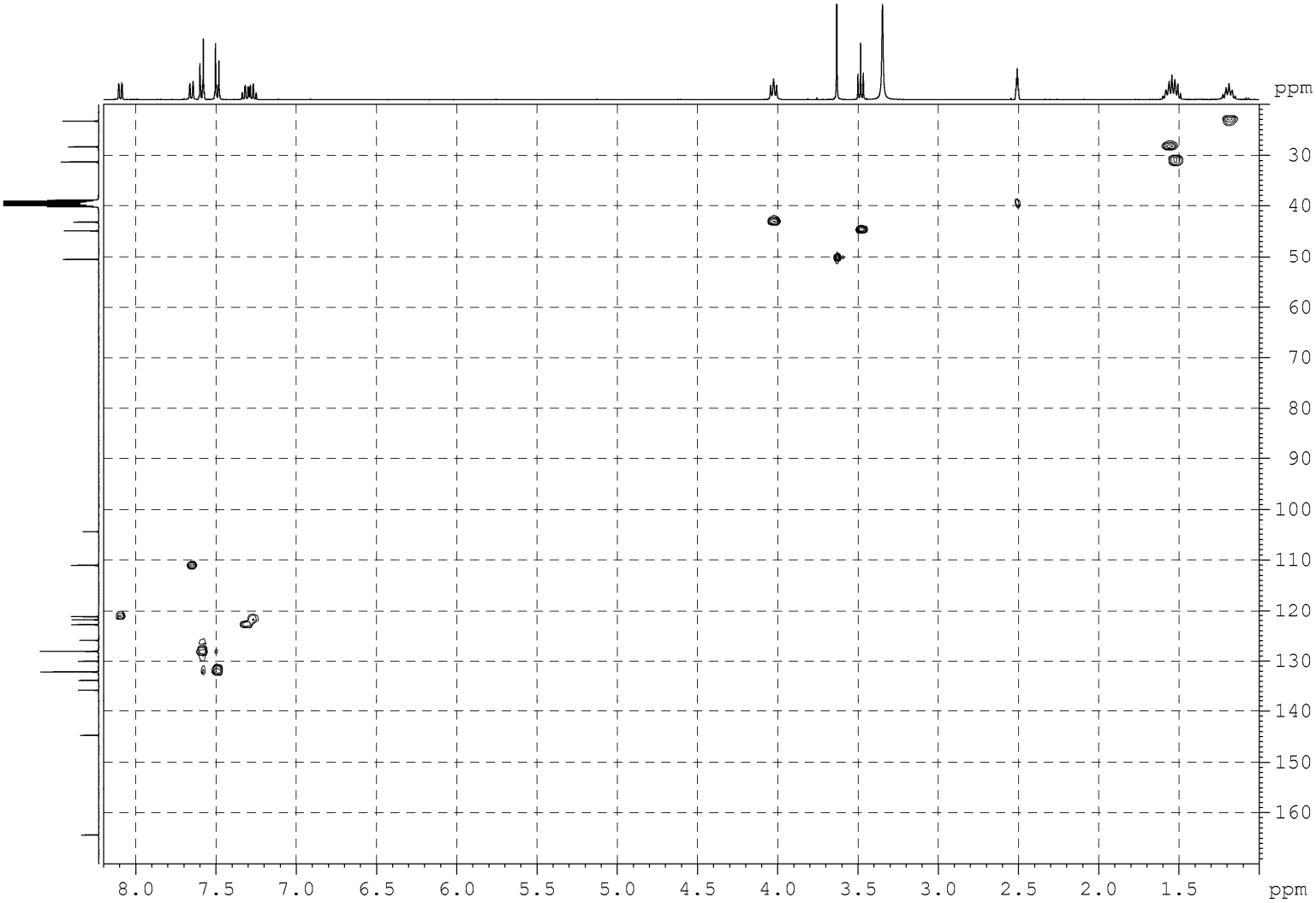

Figure S133. 2D ^{1}H-^{13}C HSQC NMR spectra of **11b** in DMSO at T = 303 K.

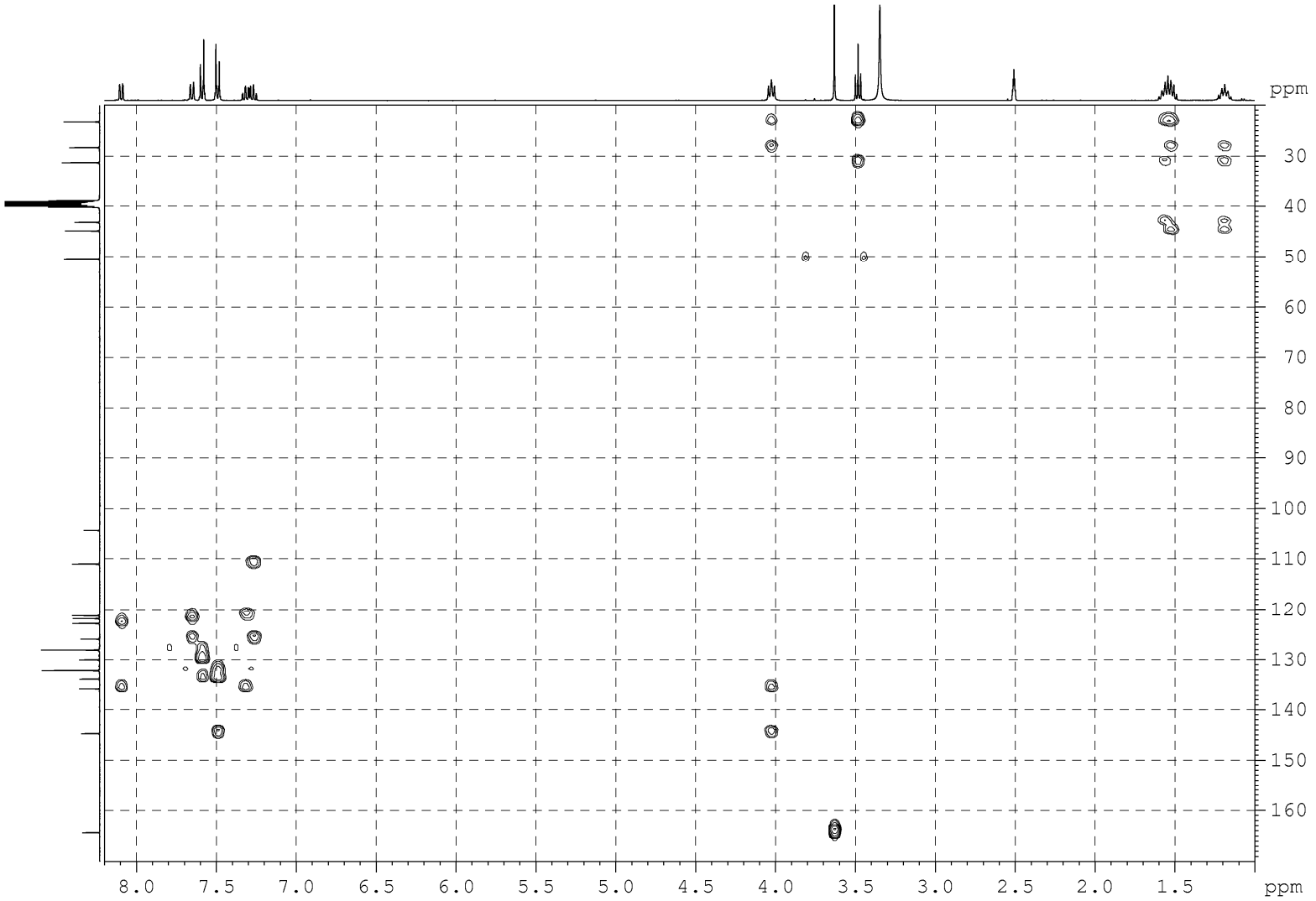

Figure S134. 2D ^{1}H-^{13}C HMBC NMR spectra of **11b** in DMSO at T = 303 K.

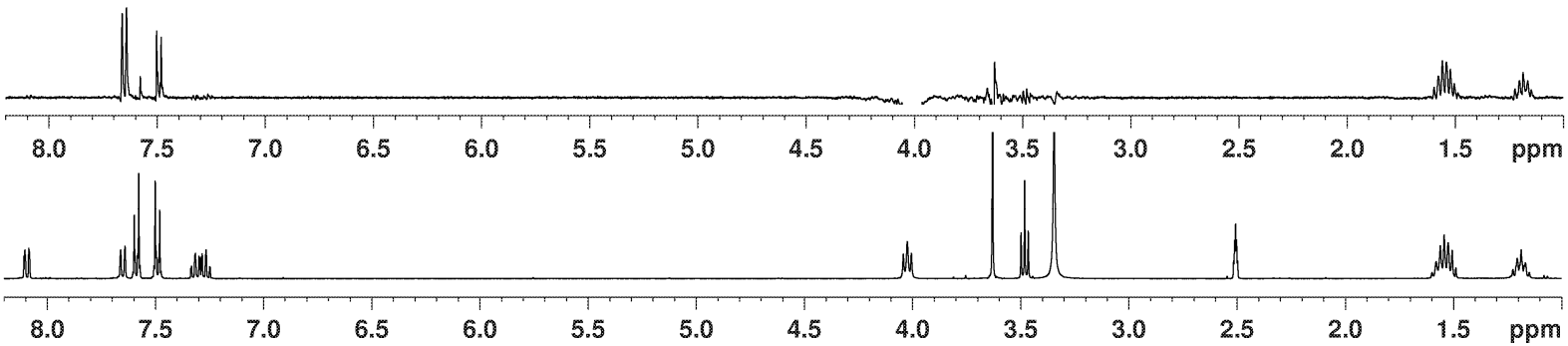

Figure S135. 1D ^{1}H and ^{1}H DPFGROE NMR spectra of **11b** in DMSO at T = 303 K.

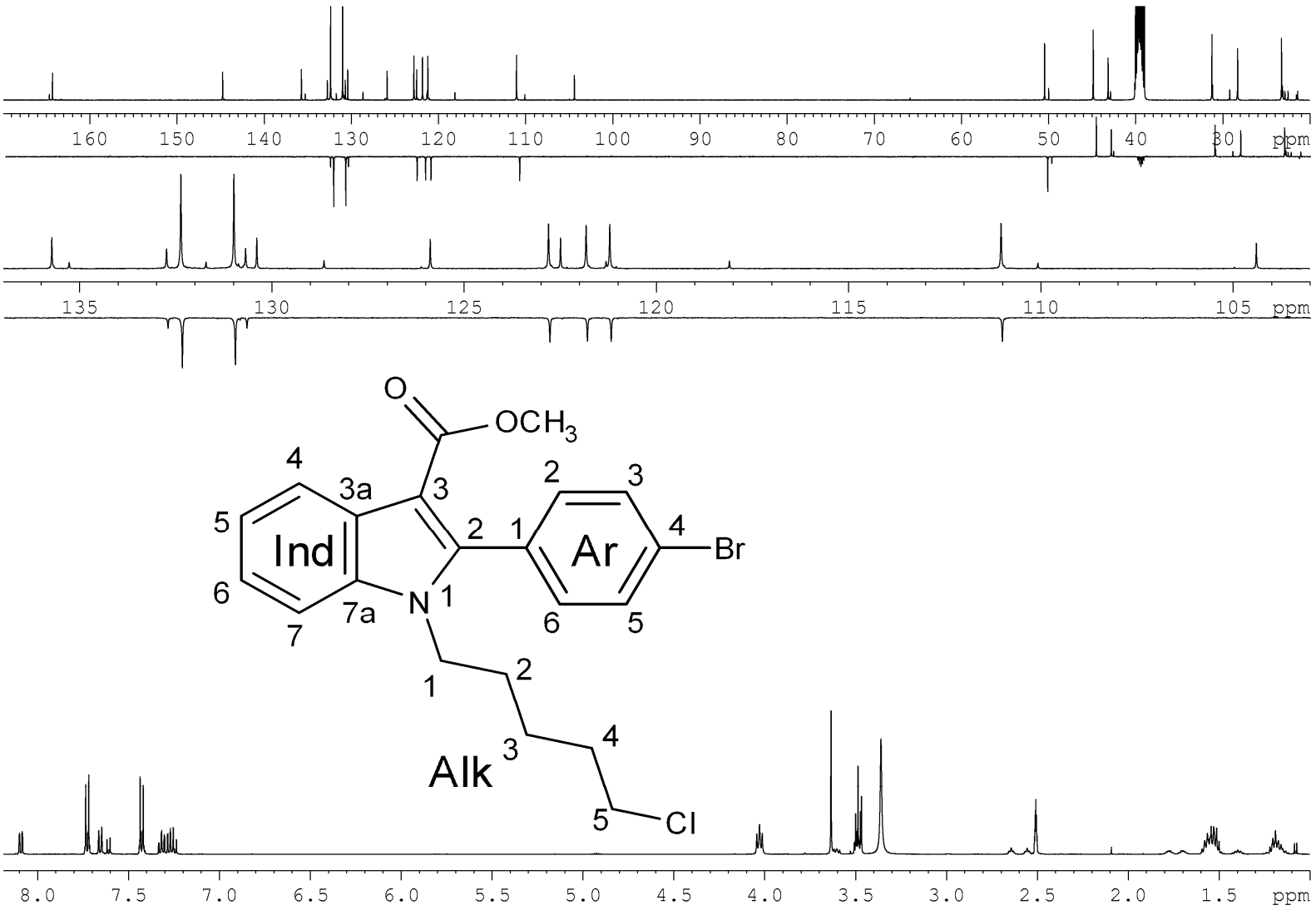

Figure S136. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **11c** in DMSO at T = 303 K.

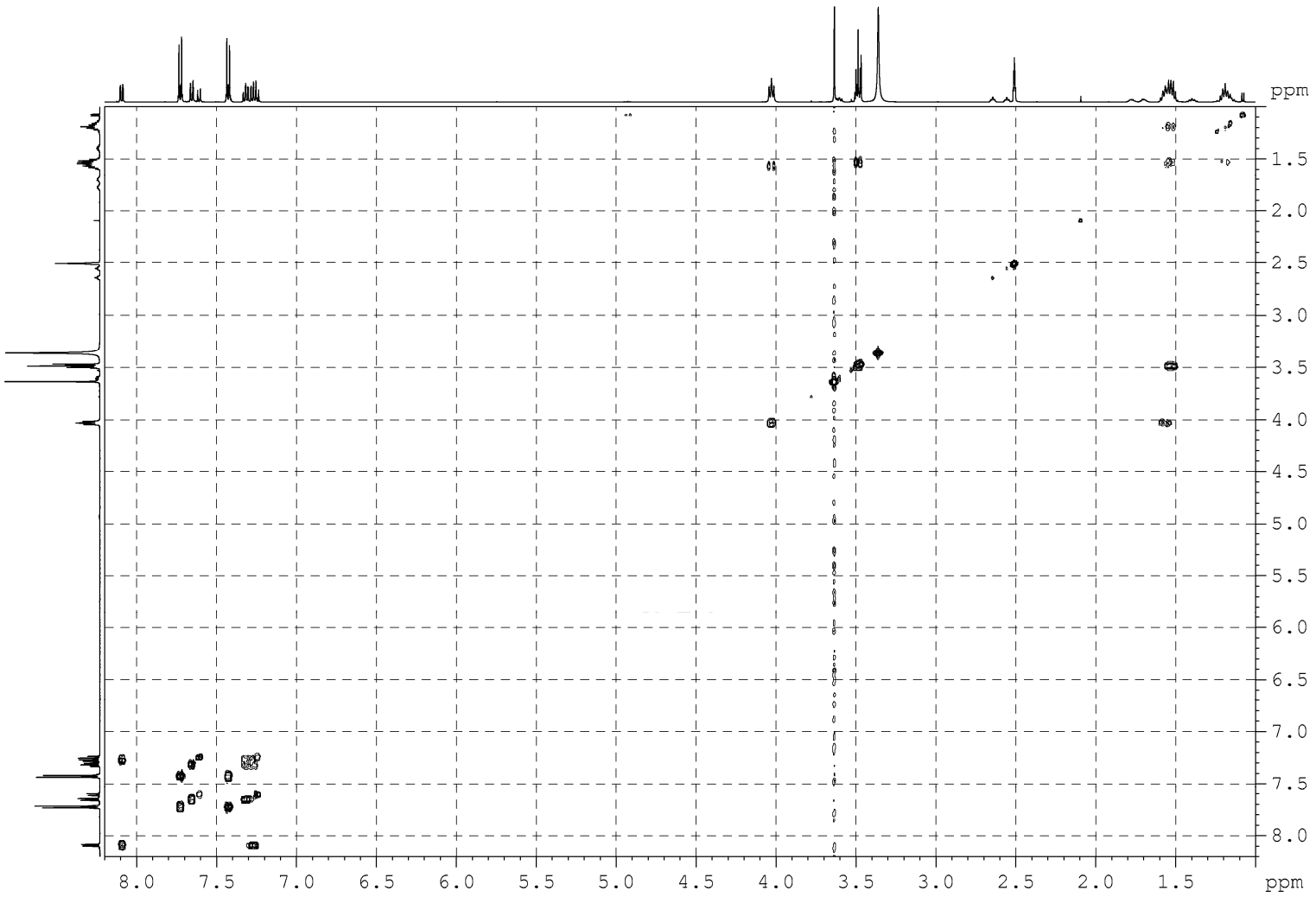

Figure S137. 2D ^{1}H-^{1}H COSY NMR spectra of **11c** in DMSO at T = 303 K.

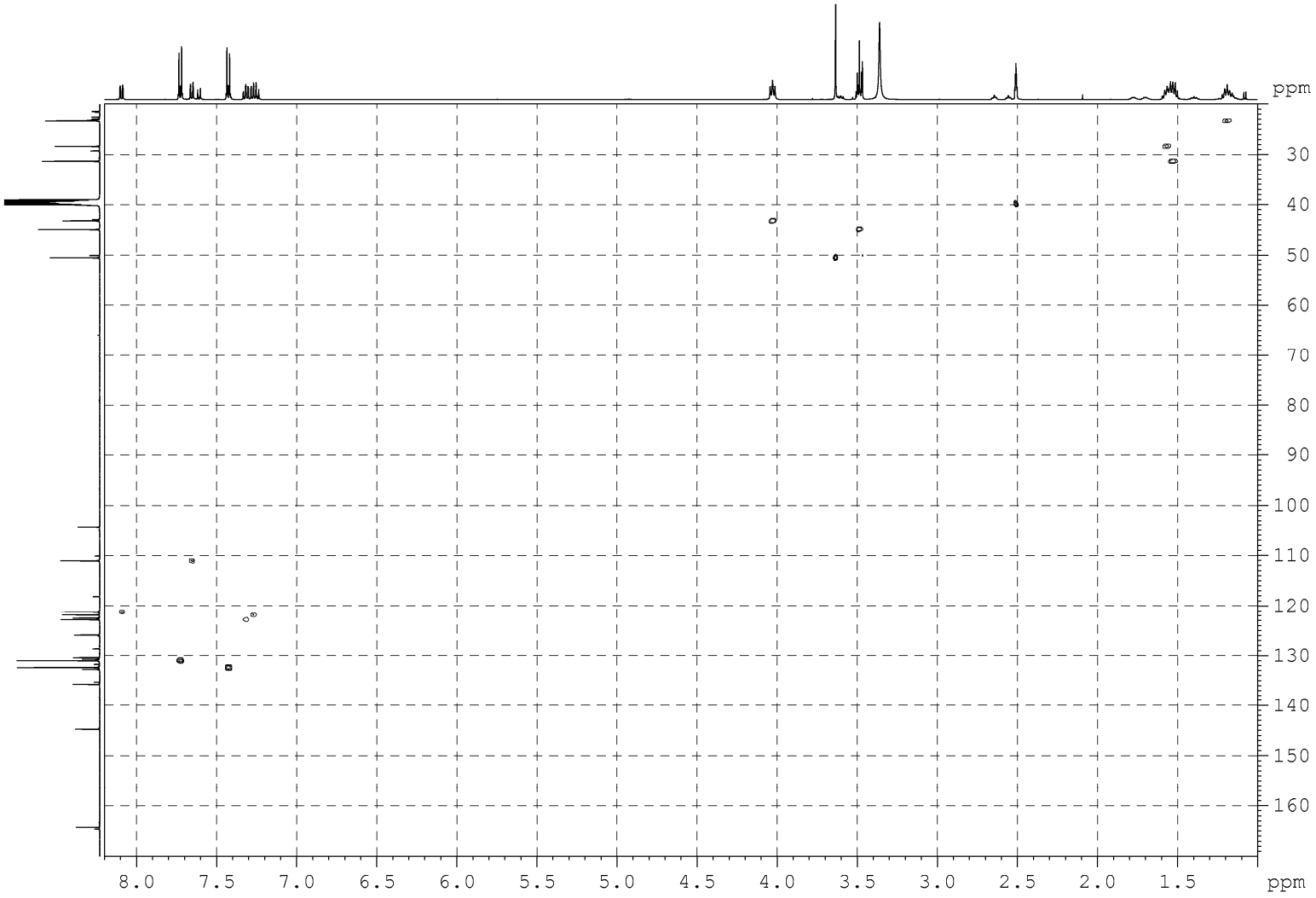

Figure S138. 2D ^{1}H-^{13}C HSQC NMR spectra of **11c** in DMSO at T = 303 K.

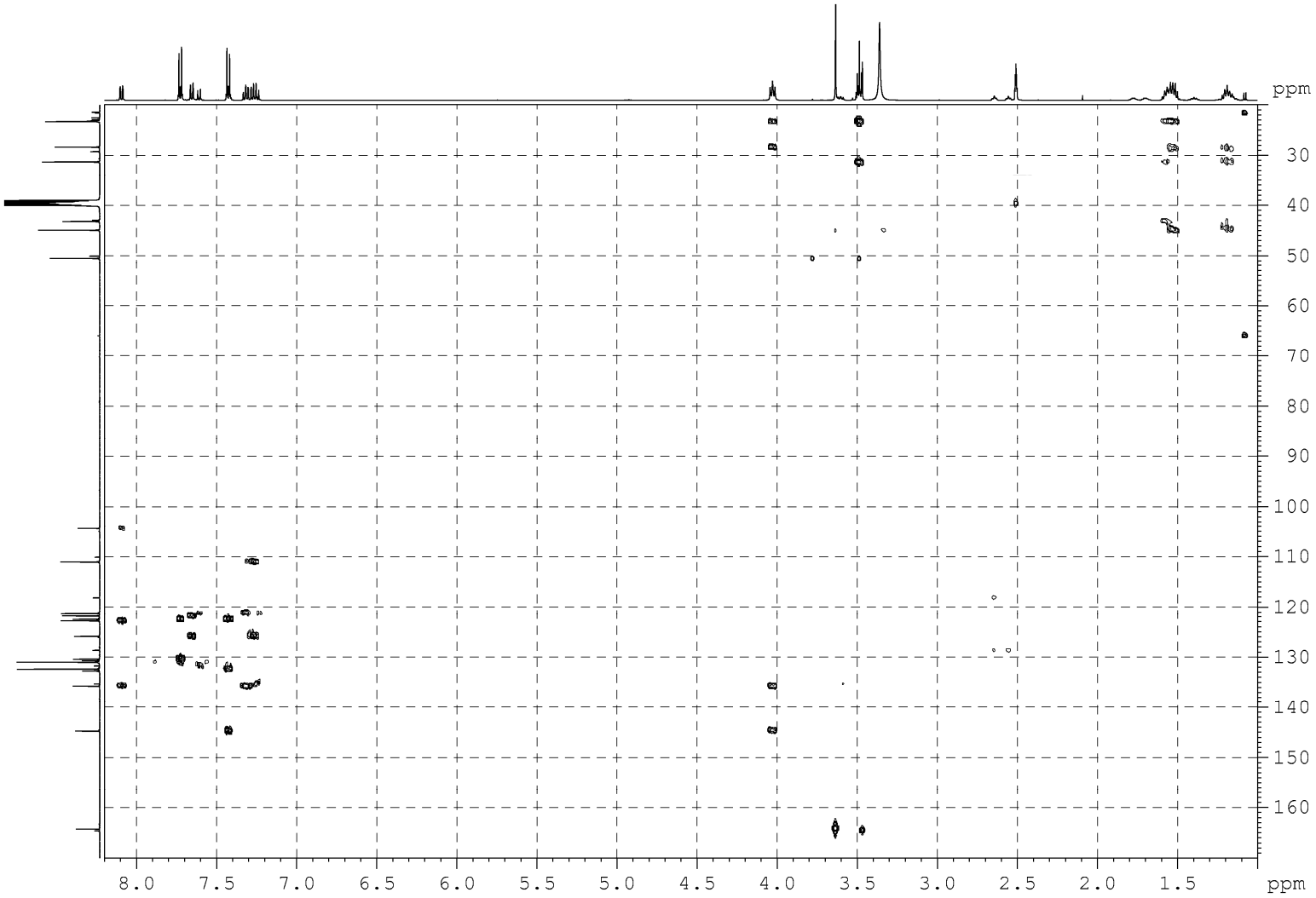

Figure S139. 2D ^{1}H-^{13}C HMBC NMR spectra of **11c** in DMSO at T = 303 K.

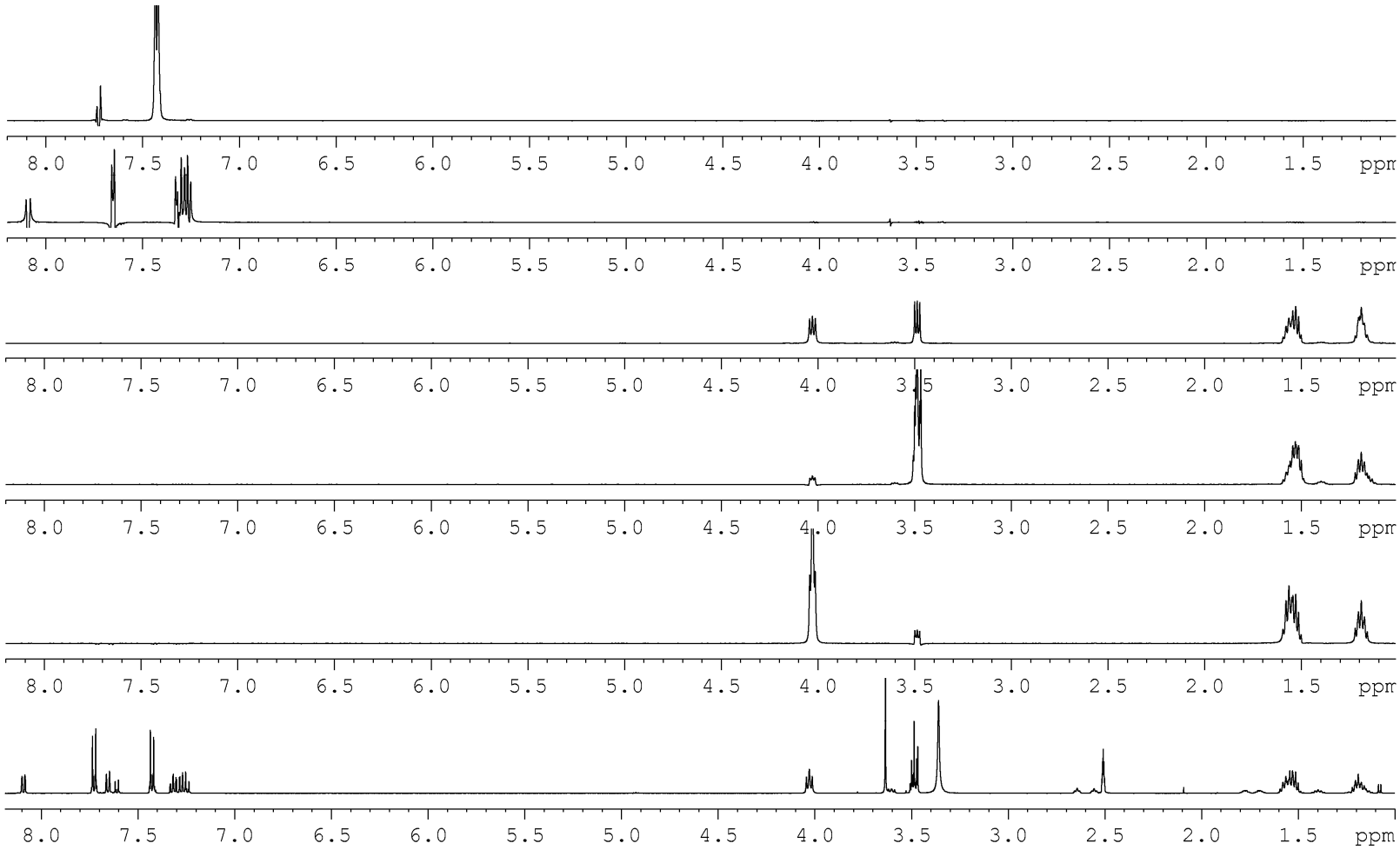

Figure S140. 1D ^{1}H and ^{1}H TOCSY NMR spectra of **11c** in DMSO at T = 303 K.

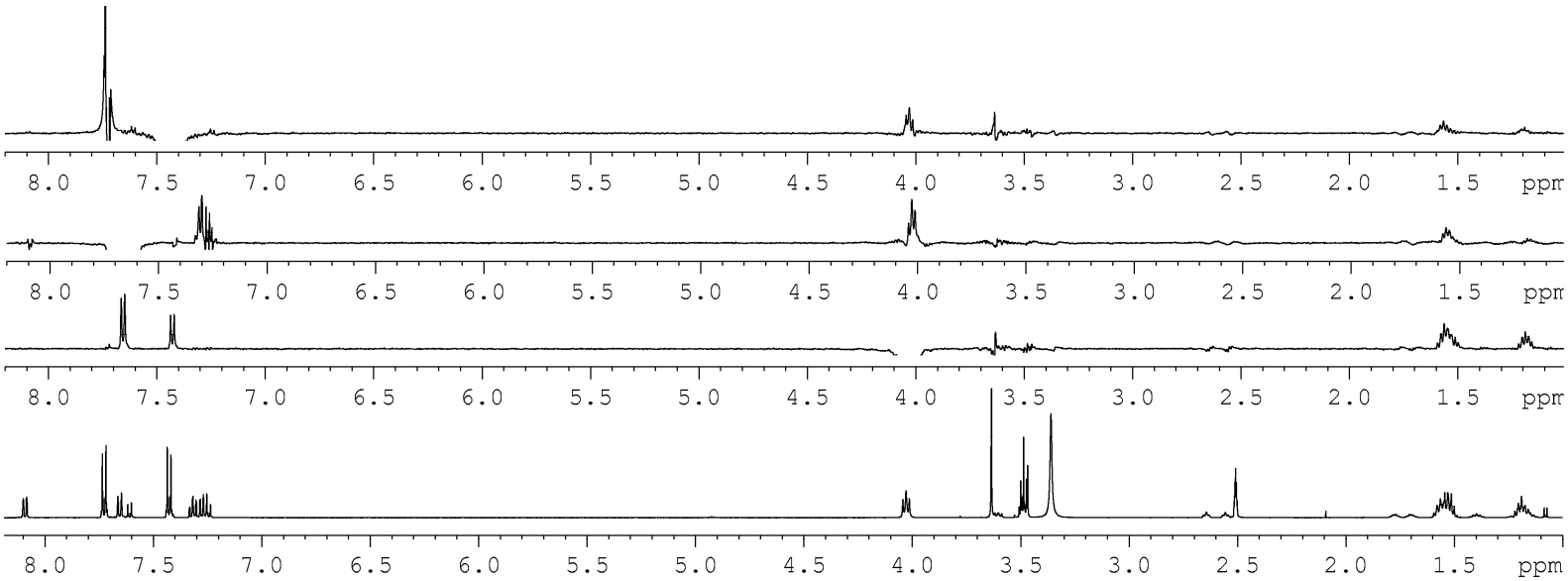

Figure S141. 1D ^{1}H and ^{1}H DPFGROE NMR spectra of **11c** in DMSO at T = 303 K.

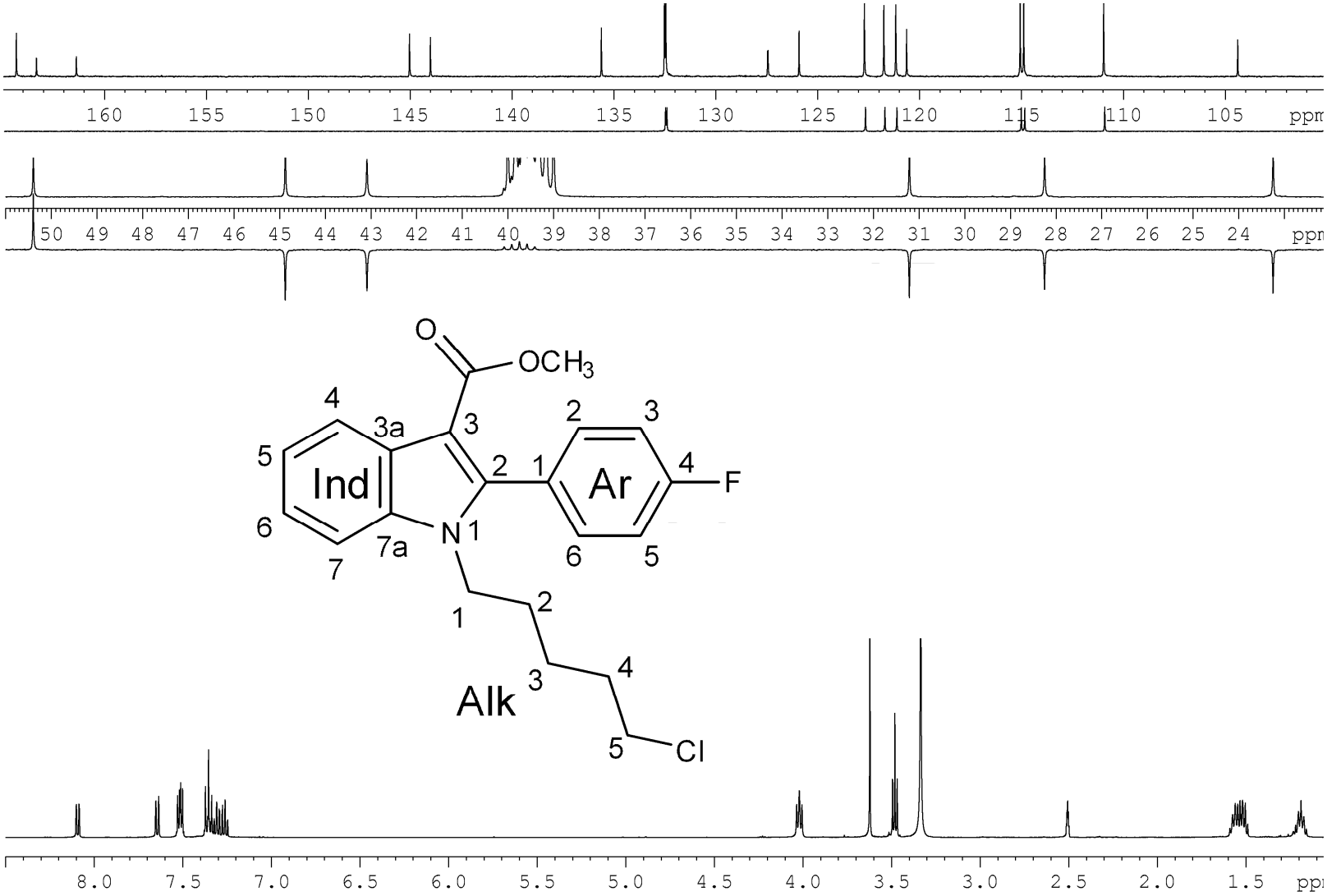

Figure S142. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **11d** in DMSO at T = 303 K.

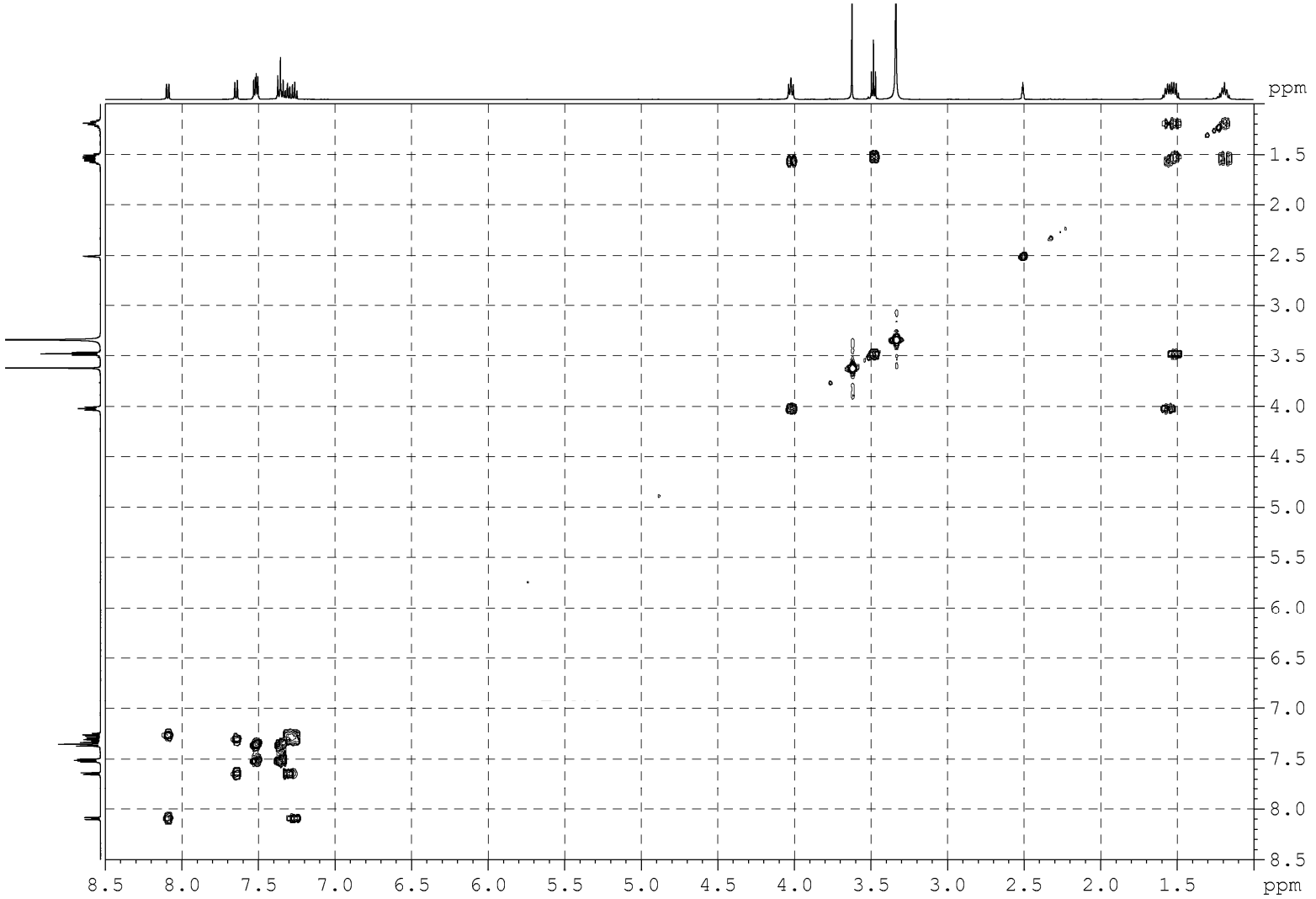

Figure S143. 2D ^{1}H-^{1}H COSY NMR spectra of **11d** in DMSO at T = 303 K.

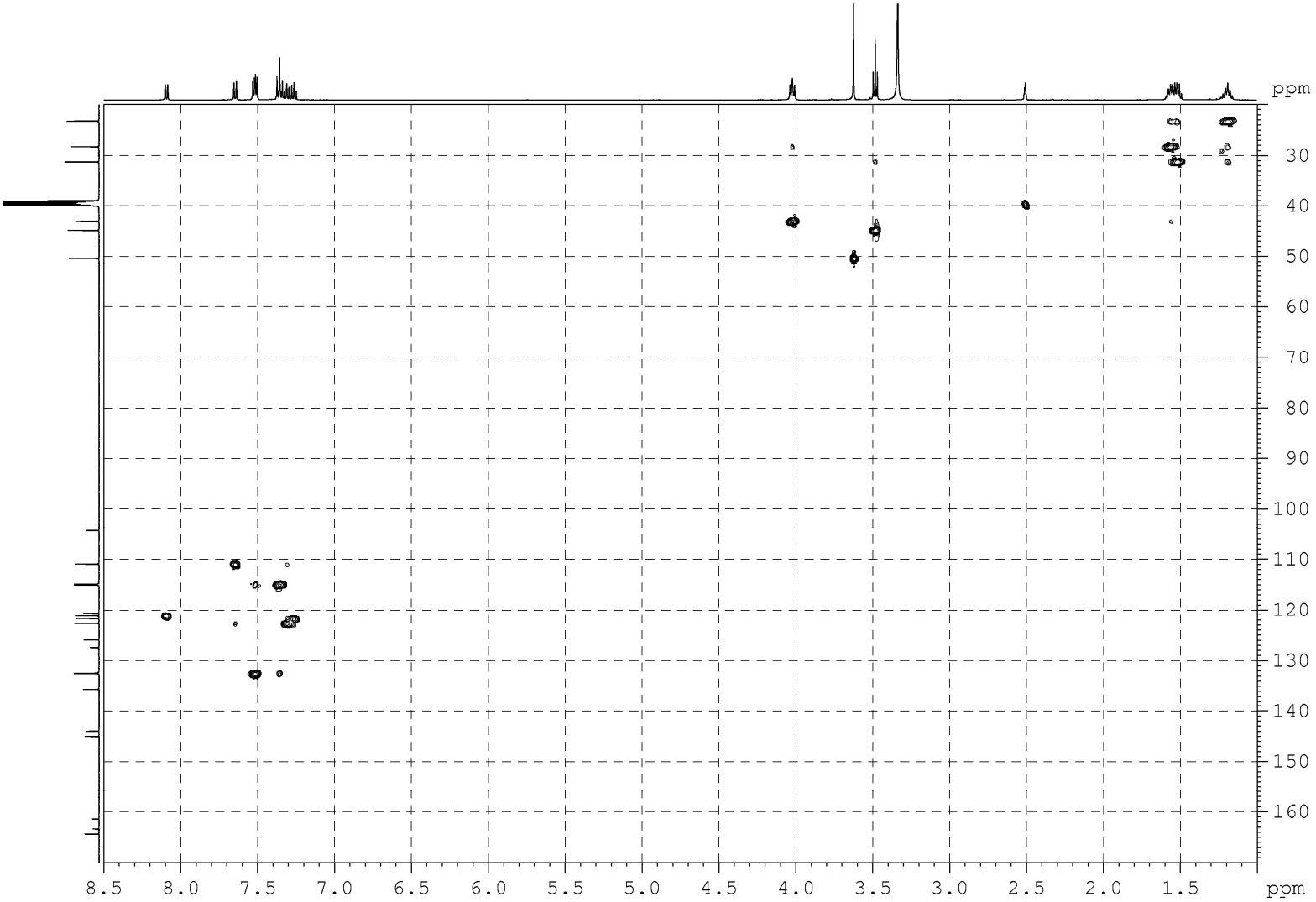

Figure S144. 2D ^{1}H-^{13}C HSQC NMR spectra of **11d** in DMSO at T = 303 K.

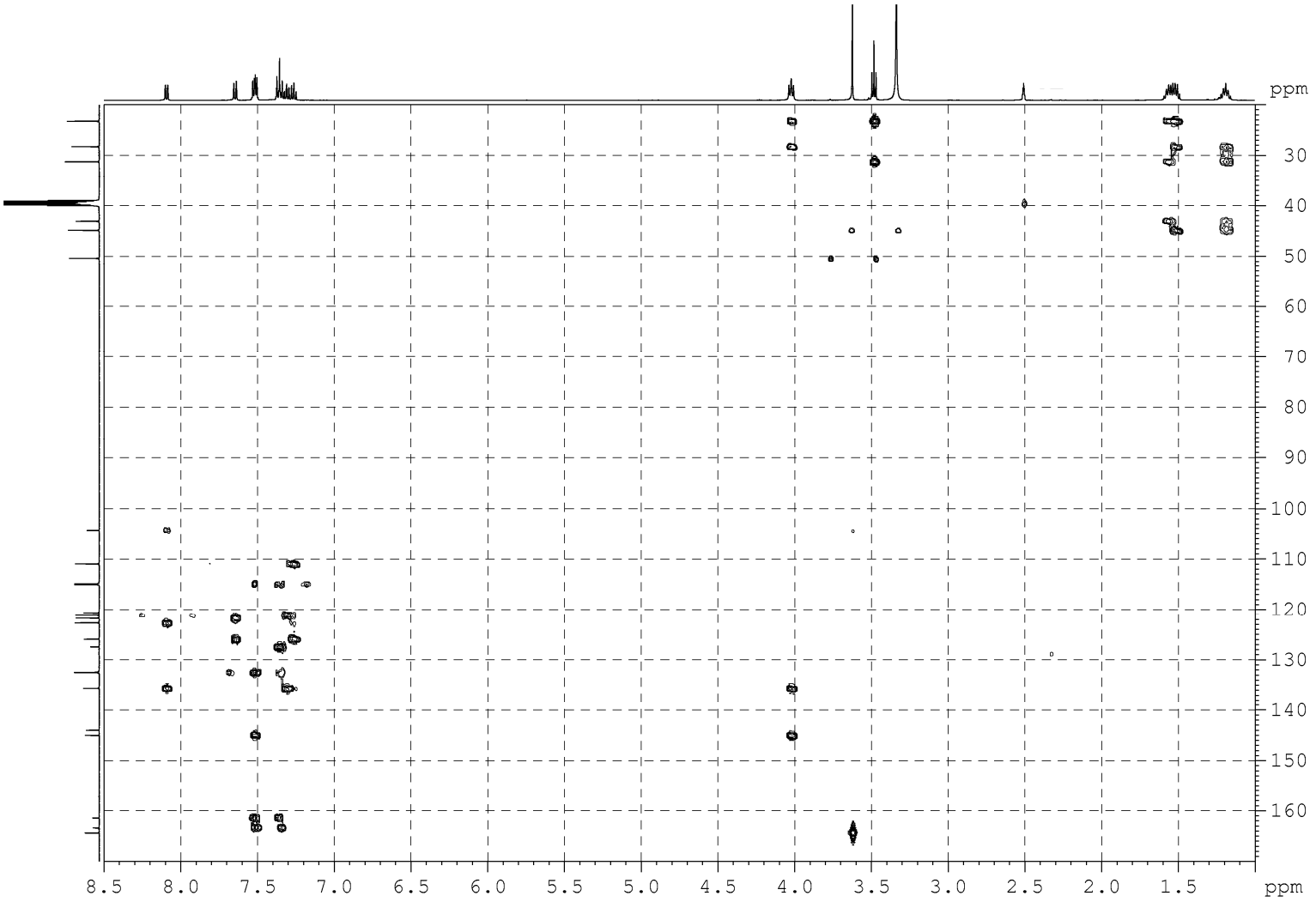

Figure S145. 2D ^{1}H-^{13}C HMBC NMR spectra of **11d** in DMSO at T = 303 K.

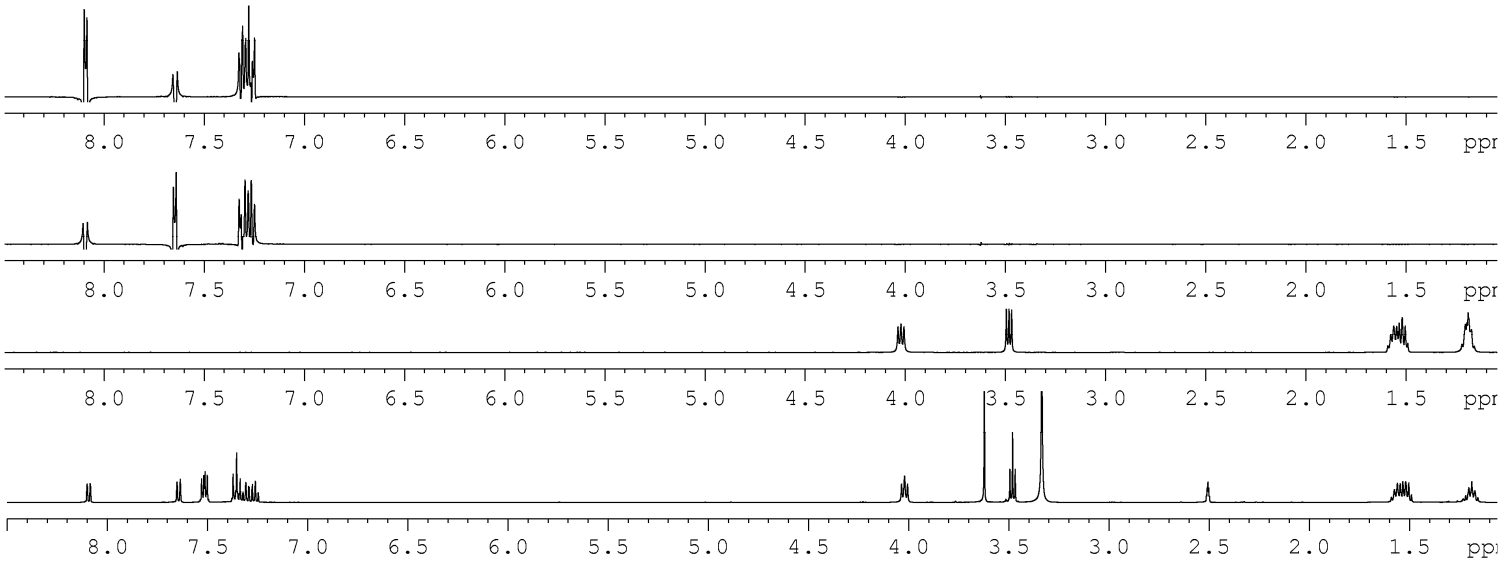

Figure S146. 1D ^{1}H and ^{1}H TOCSY NMR spectra of **11d** in DMSO at T = 303 K.

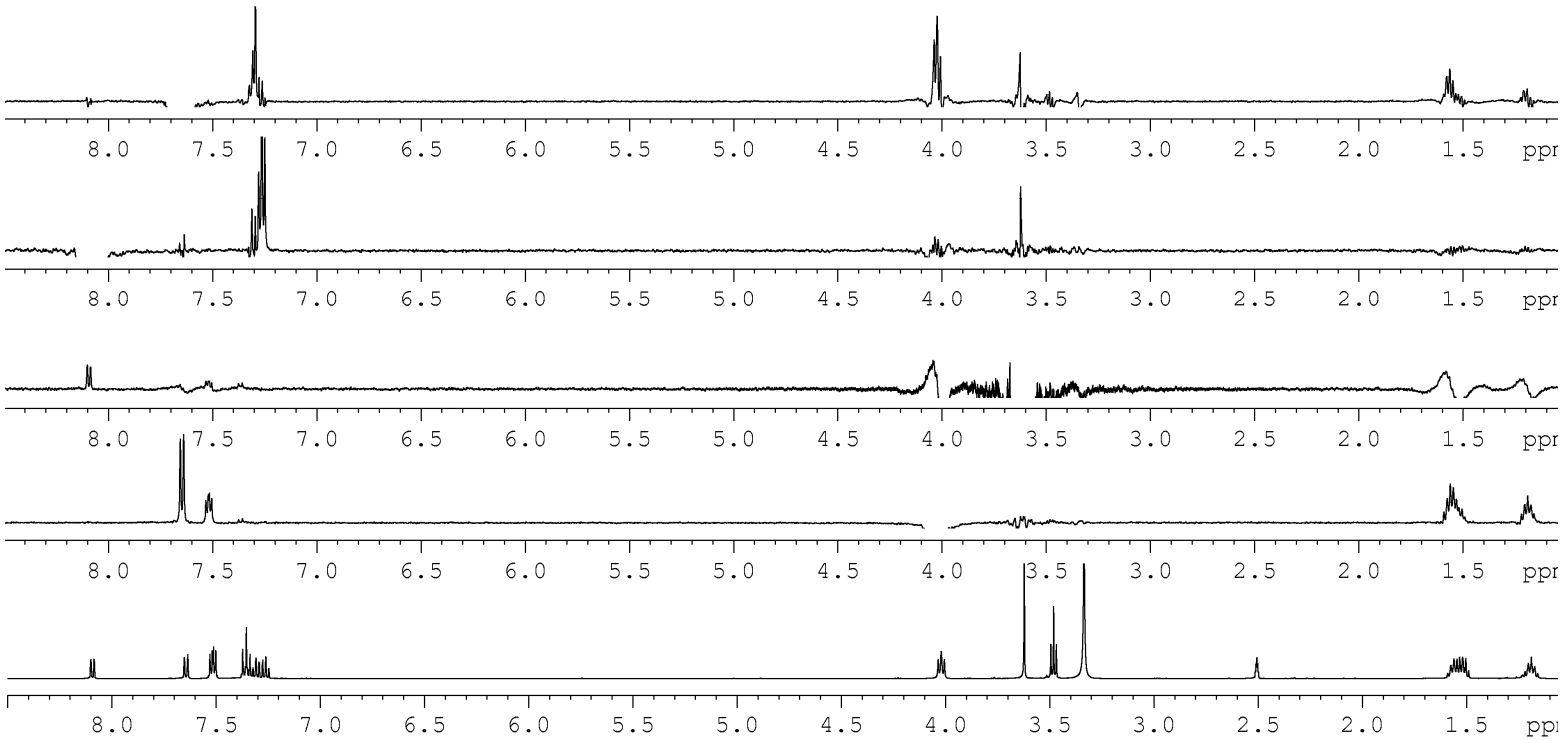

Figure S147. 1D ^{1}H and ^{1}H DPFGROE NMR spectra of **11d** in DMSO at T = 303 K.

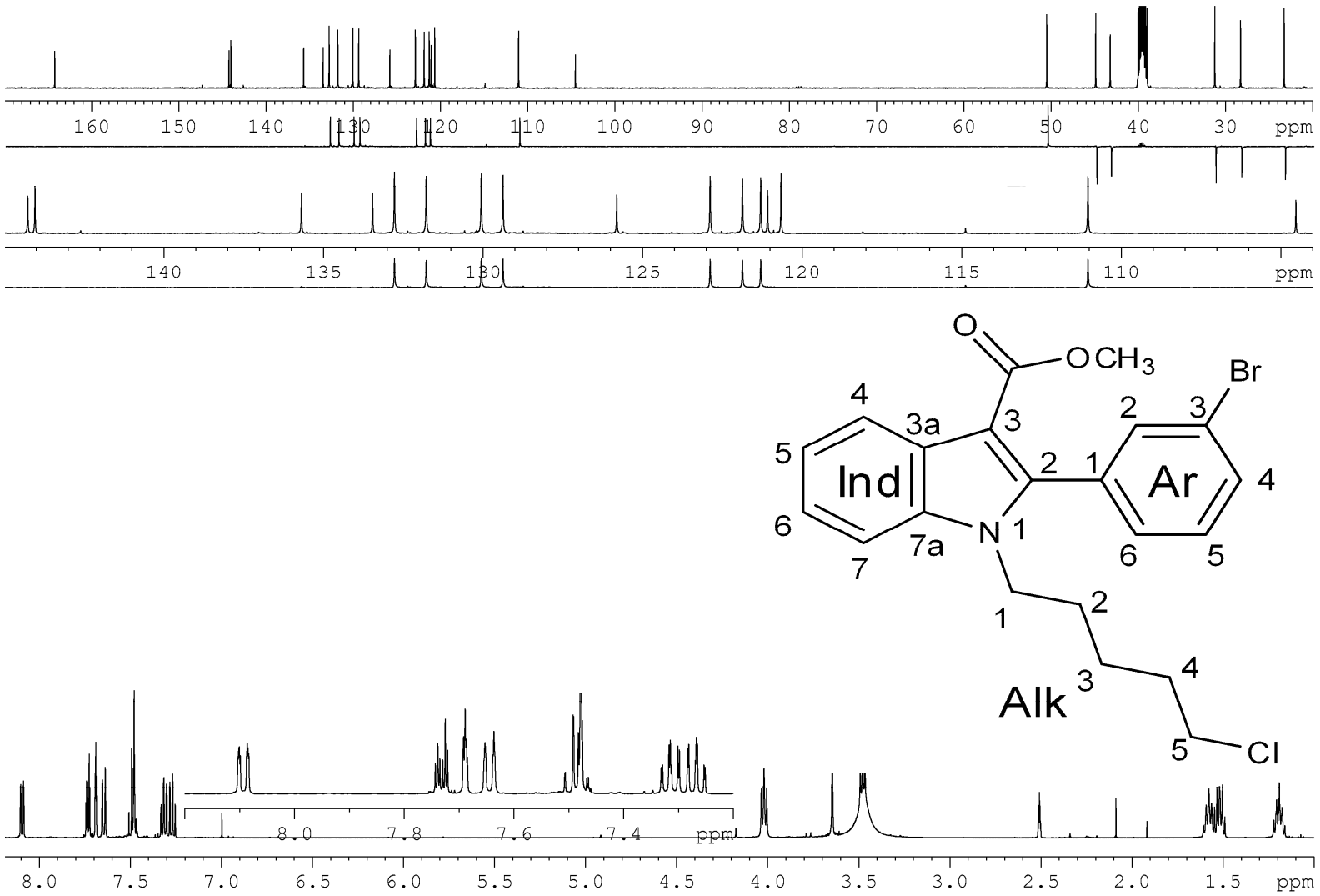

Figure S148. 1D ^{1}H, ^{13}C DEPT and ^{13}C{^{1}H} NMR spectra of **11f** in DMSO at T = 303 K.

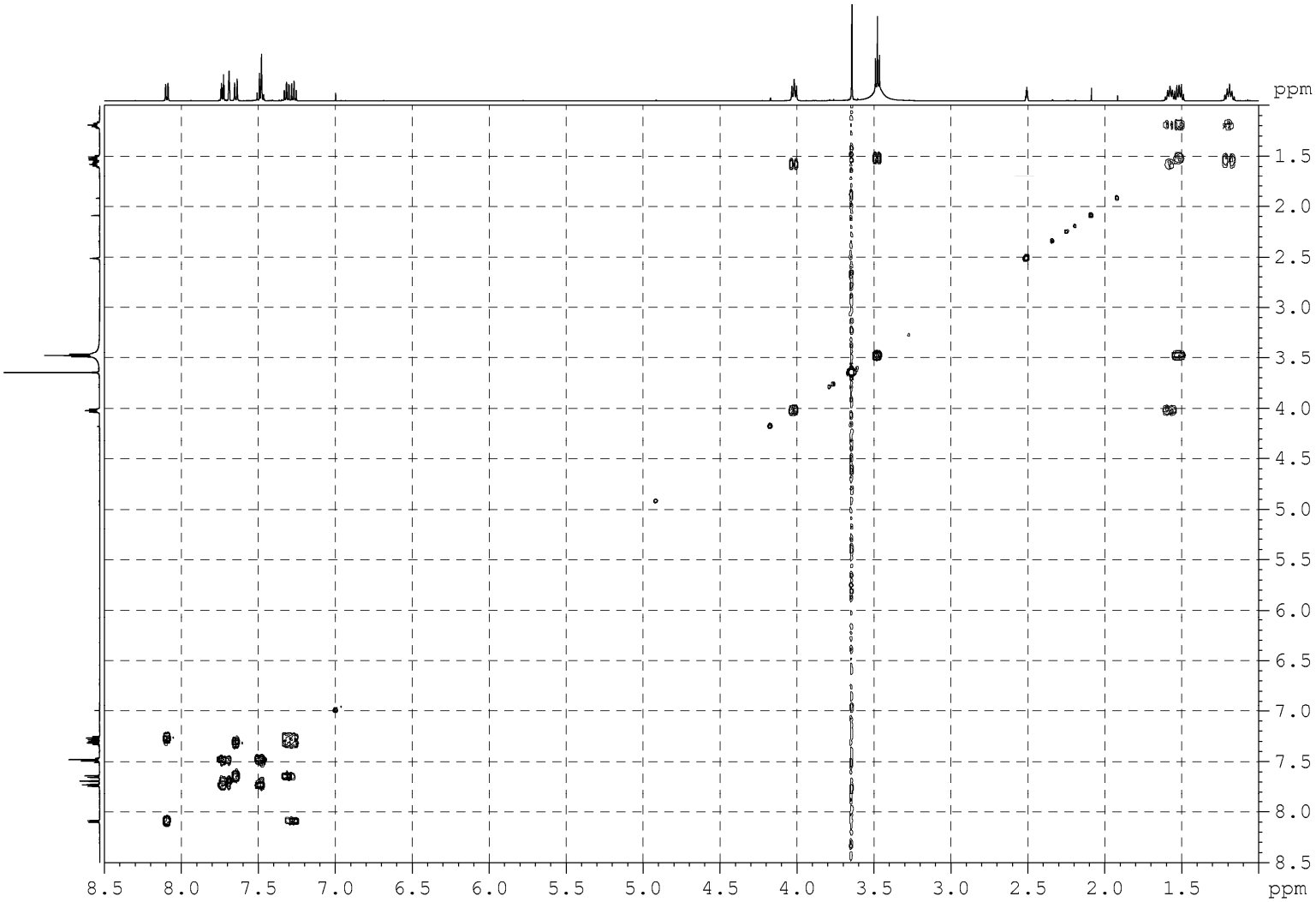

Figure S149. 2D ^{1}H-^{1}H COSY NMR spectra of **11f** in DMSO at T = 303 K.

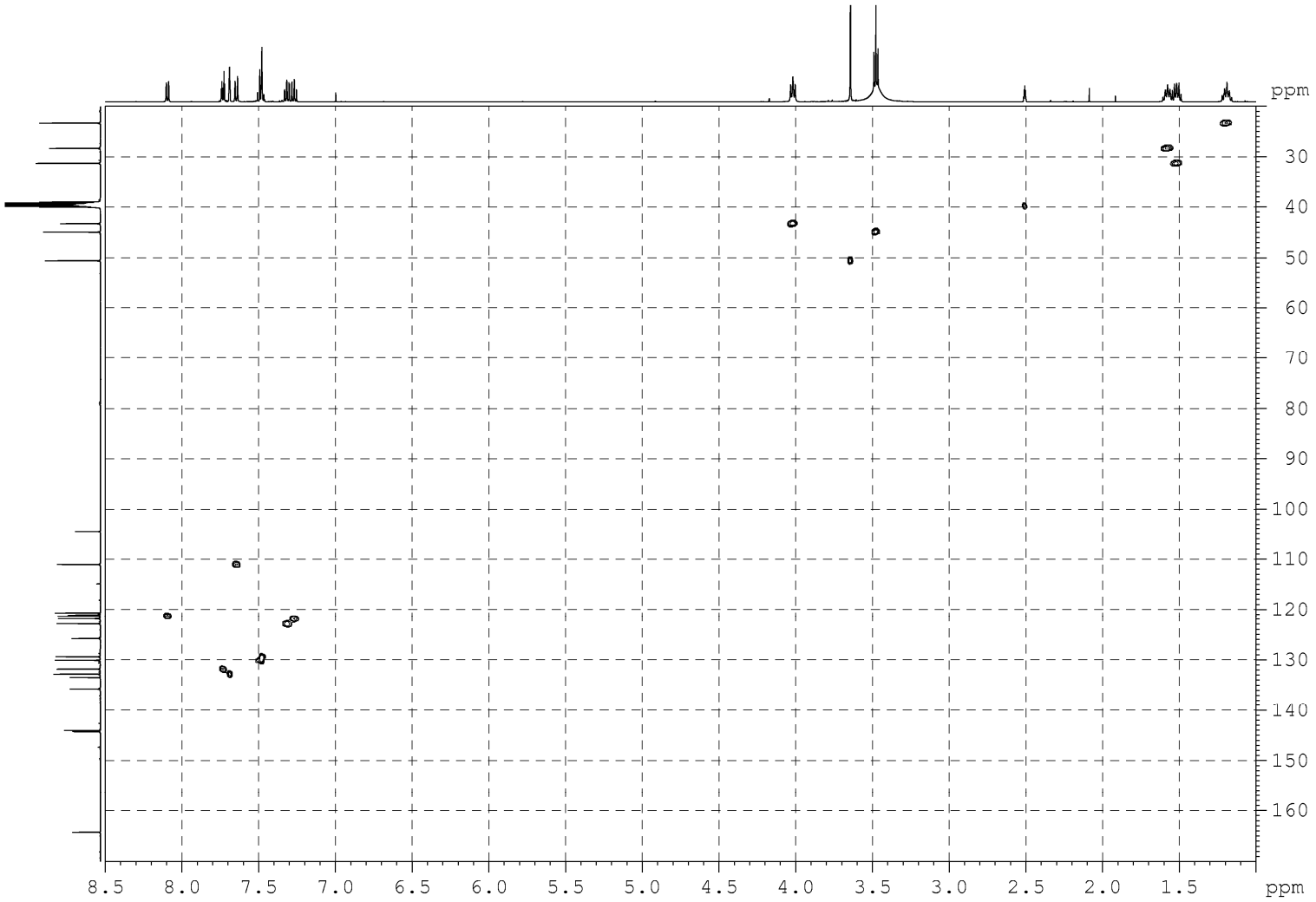

Figure S150. 2D ^{1}H-^{13}C HSQC NMR spectra of **11f** in DMSO at T = 303 K.

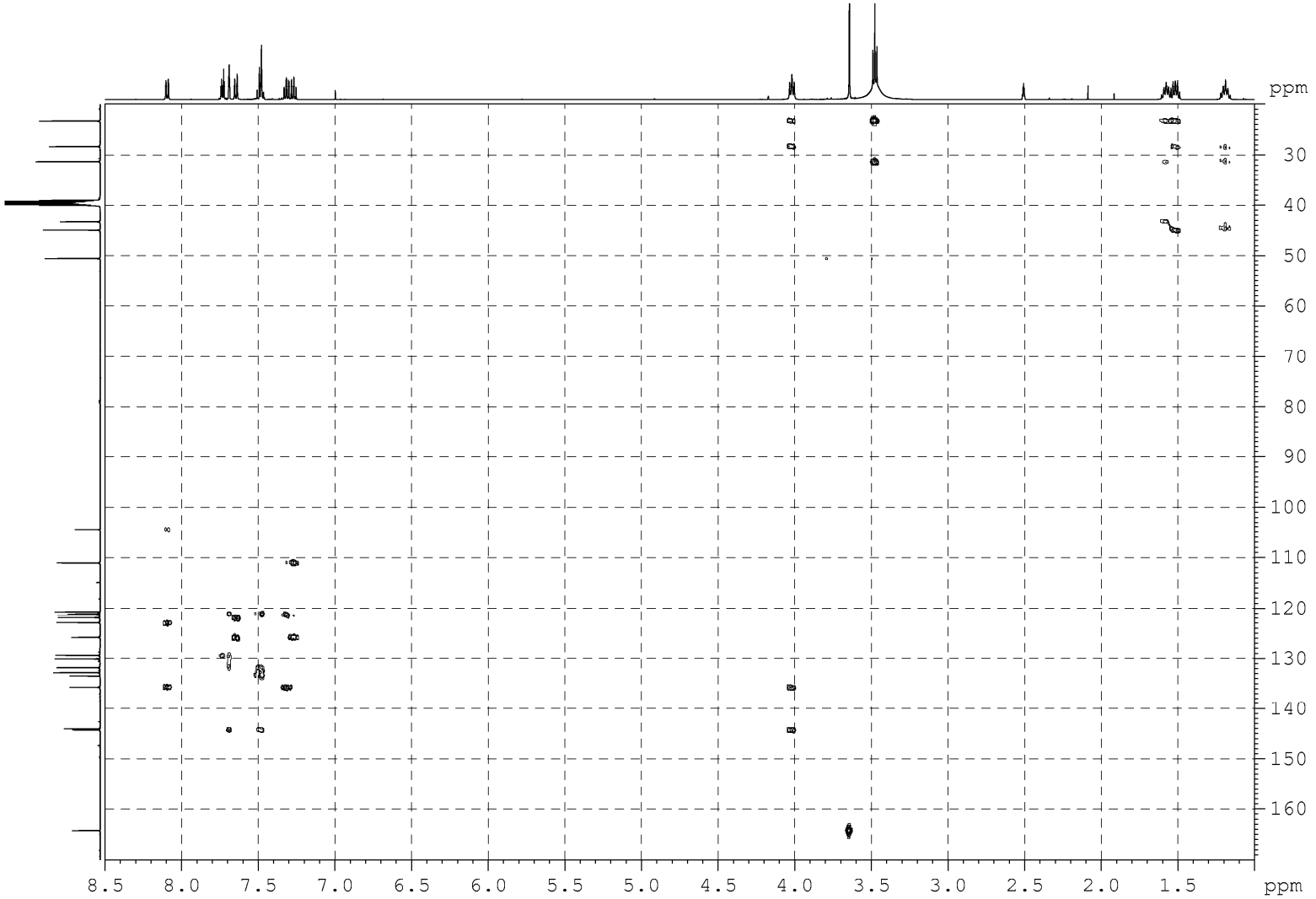

Figure S151. 2D ^{1}H-^{13}C HMBC NMR spectra of **11f** in DMSO at T = 303 K.

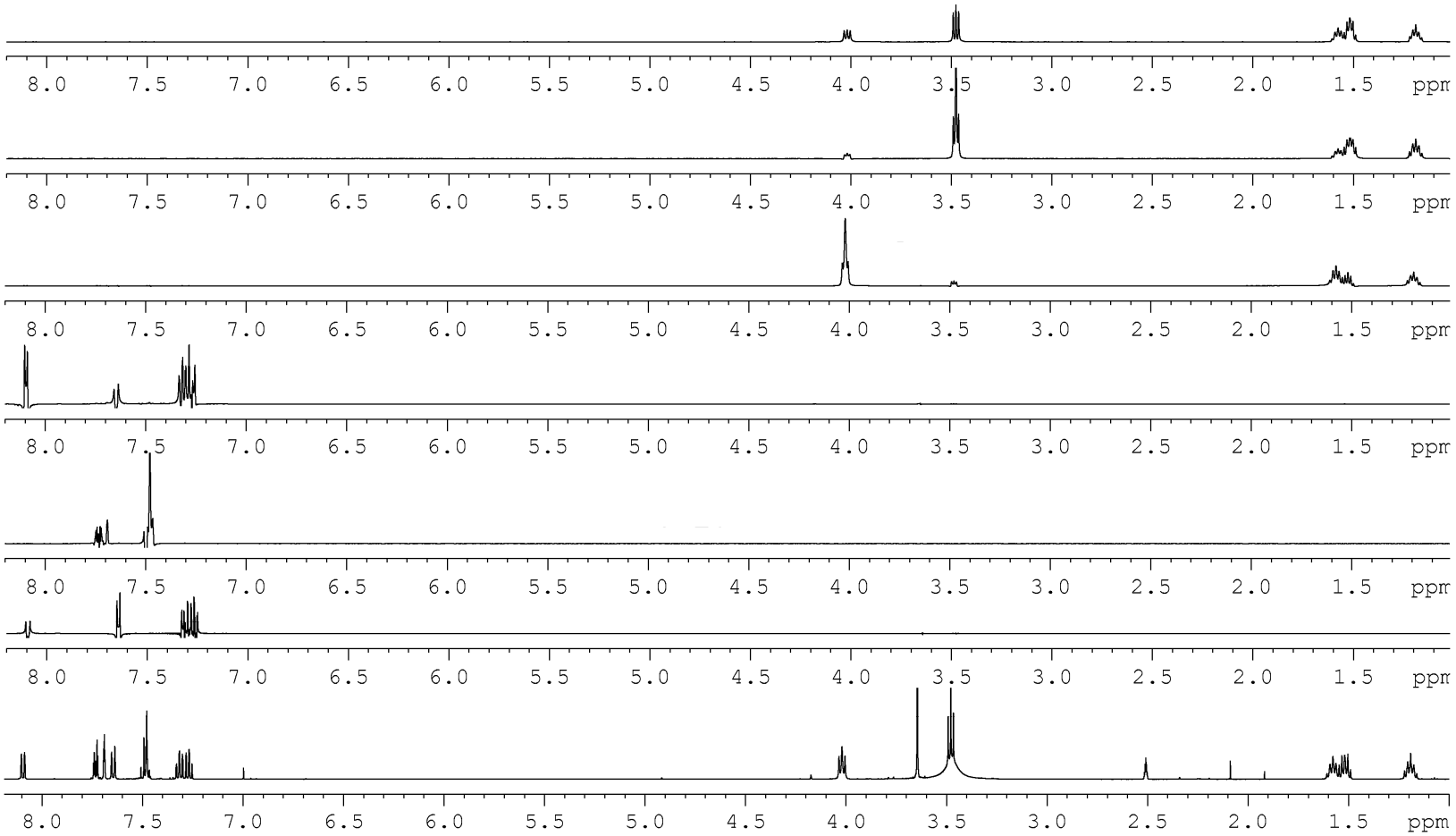

Figure S152. 1D ^{1}H and ^{1}H TOCSY NMR spectra of **11f** in DMSO at T = 303 K.

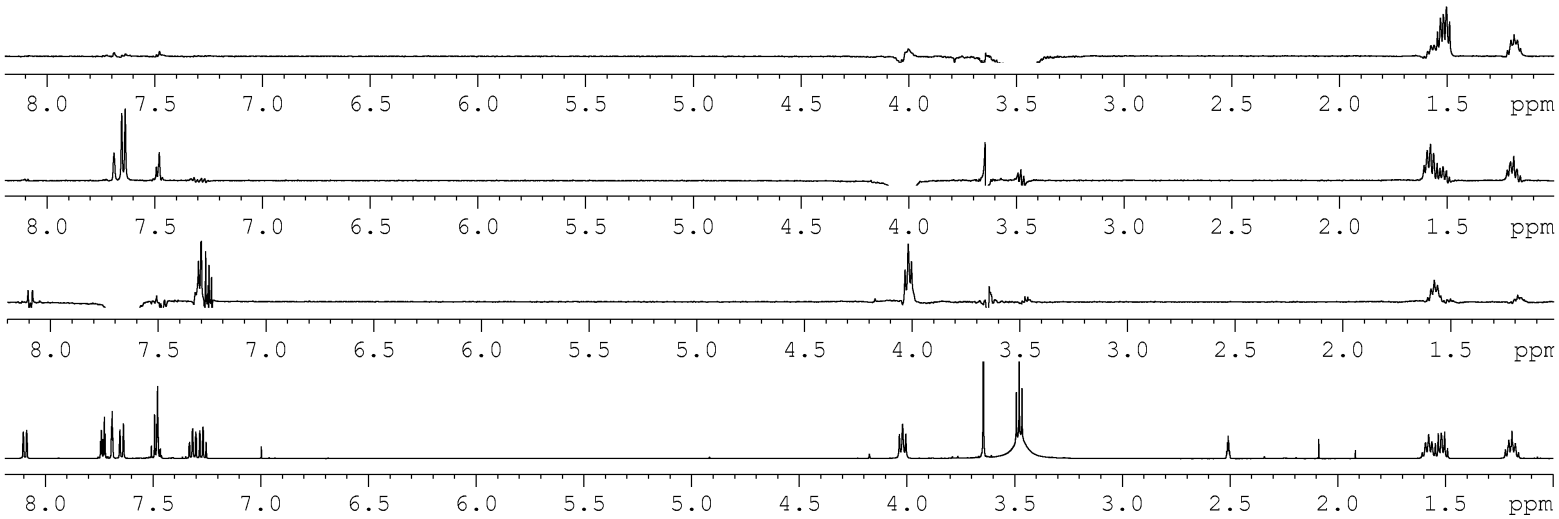

Figure S153. 1D ^{1}H and ^{1}H DPFGROE NMR spectra of **11f** in DMSO at T = 303 K.

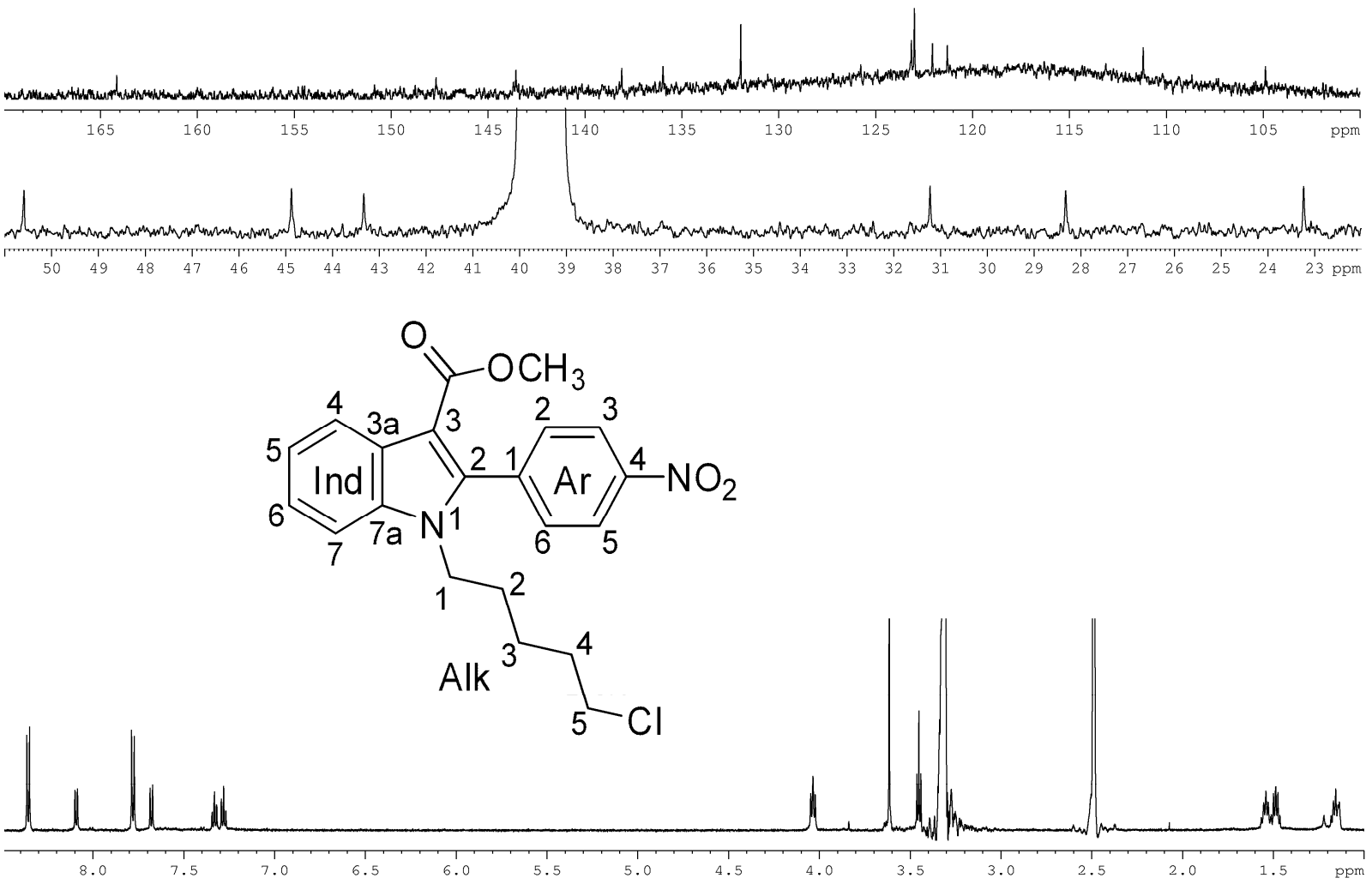

Figure S154. 1D ^{1}H, ^{13}C DEPT and $^{13}C\{^{1}H\}$ NMR spectra of **11g** in DMSO at T = 303 K.

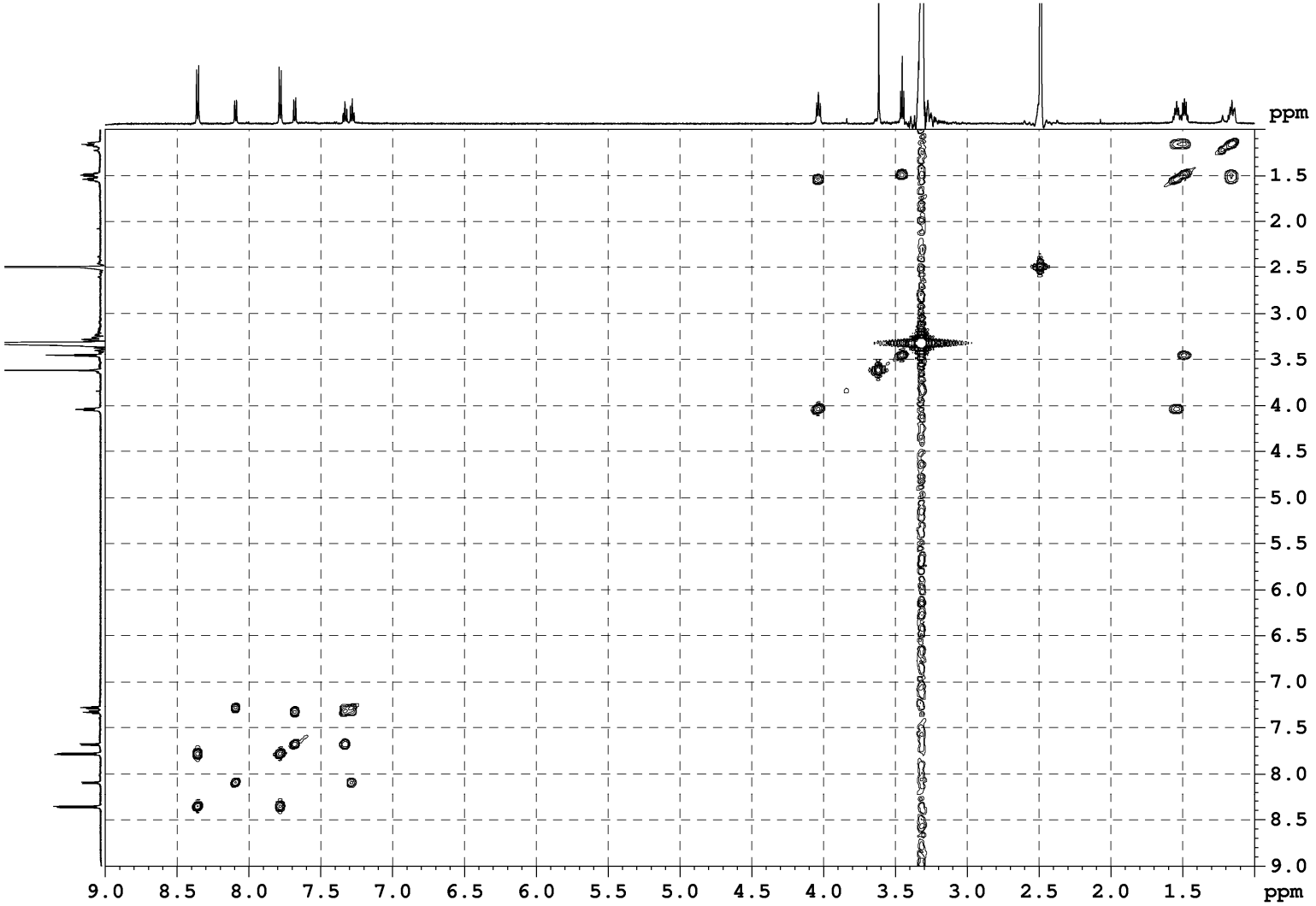

Figure S155. 2D ^{1}H-^{1}H COSY NMR spectra of **11g** in DMSO at T = 303 K.

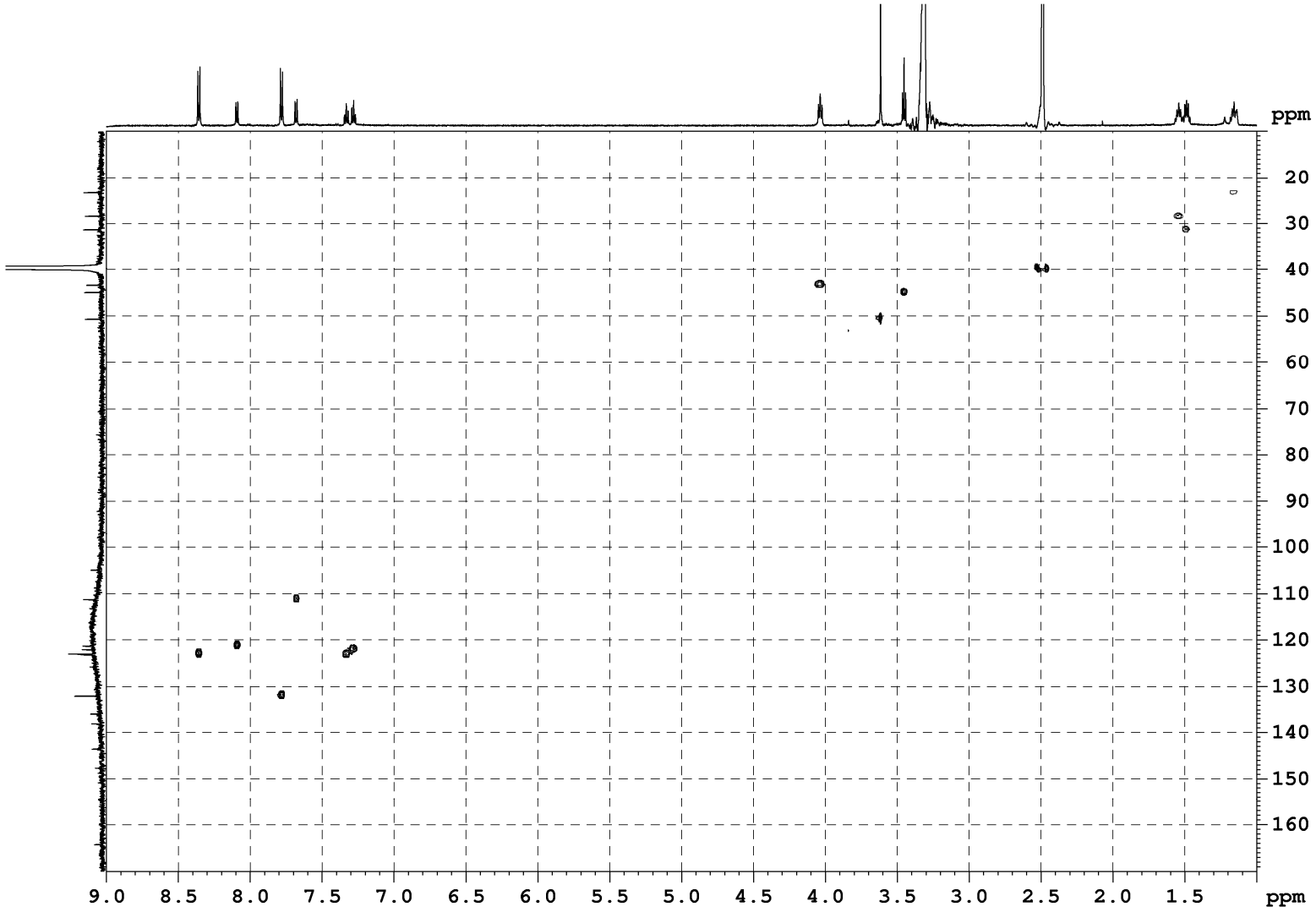

Figure S156. 2D ^{1}H-^{13}C HSQC NMR spectra of **11g** in DMSO at T = 303 K.

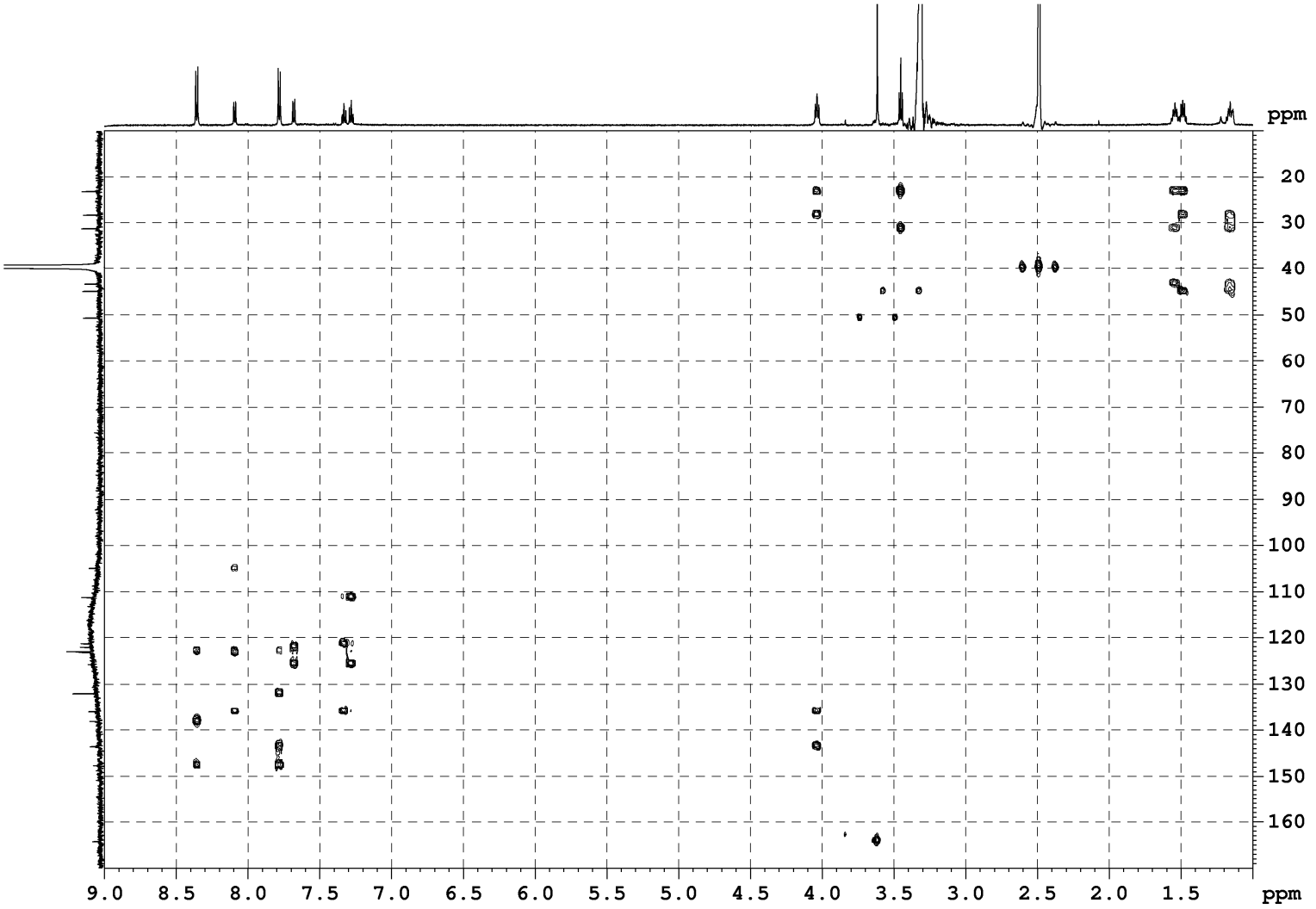

Figure S157. 2D ^{1}H-^{13}C HMBC NMR spectra of **11g** in DMSO at T = 303 K.

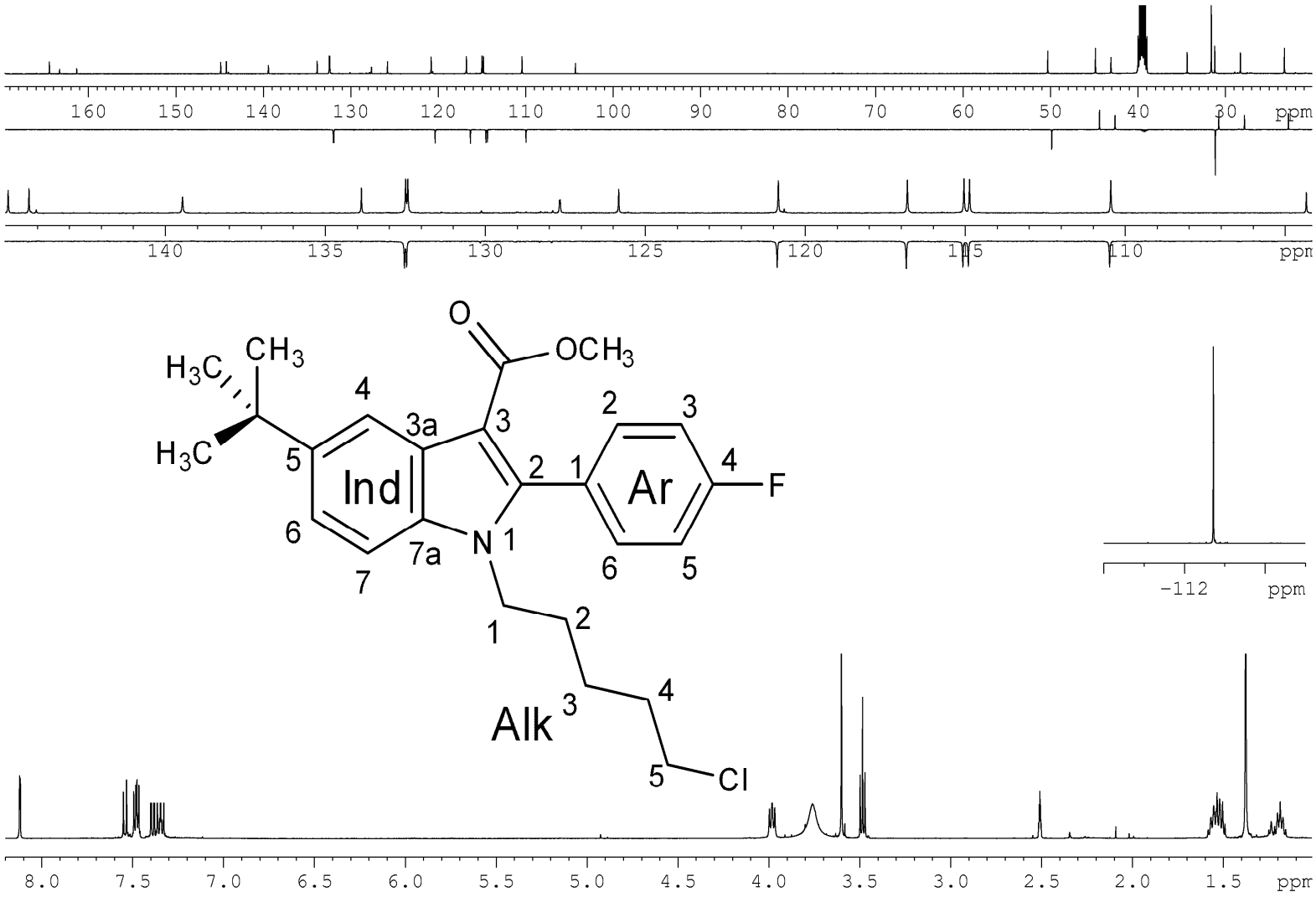

Figure S158. 1D ^{1}H, ^{13}C DEPT, ^{13}C{^{1}H} and ^{19}F{^{1}H} NMR spectra of **11i** in DMSO at T = 303 K.

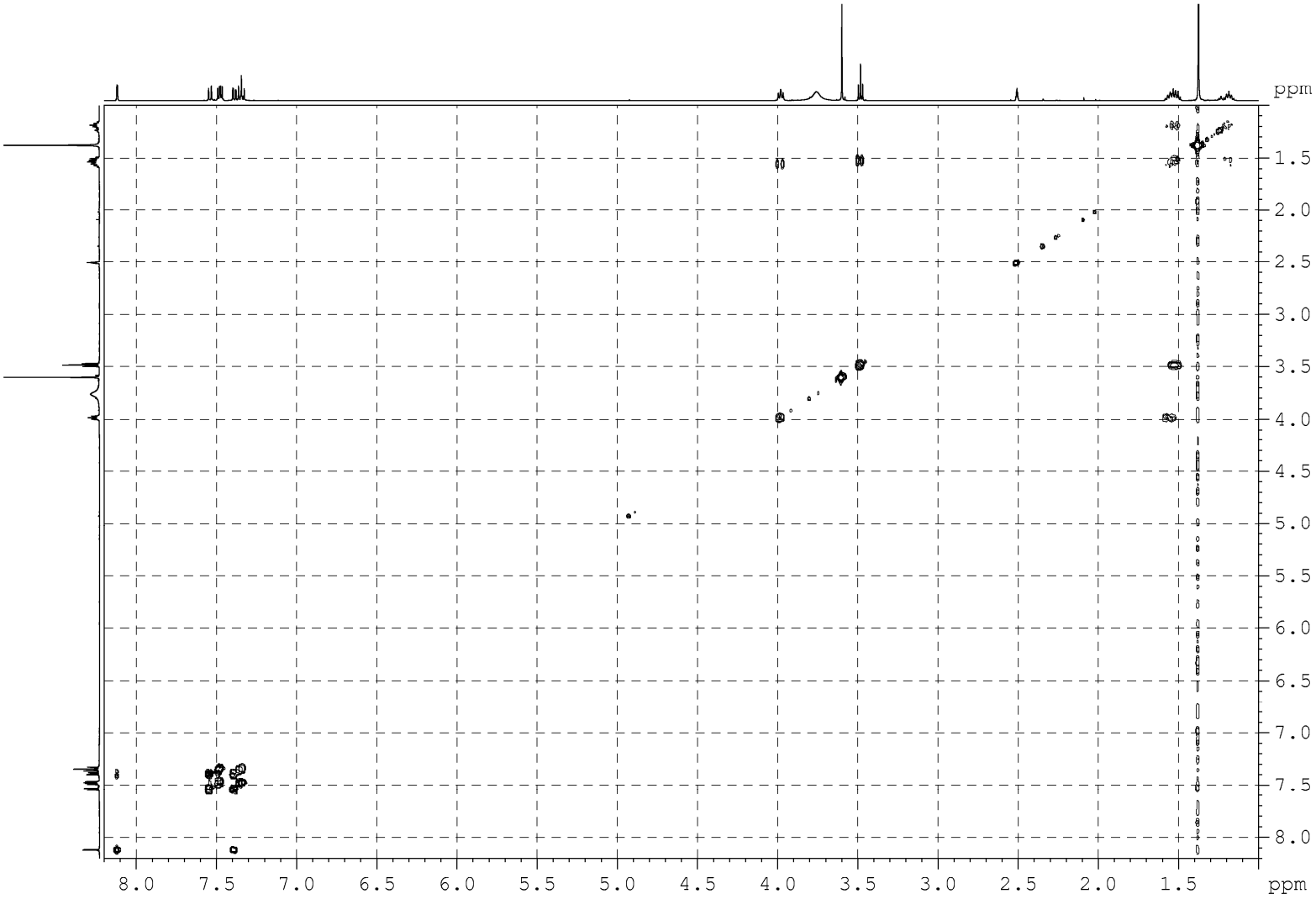

Figure S159. 2D ^{1}H-^{1}H COSY NMR spectra of **11i** in DMSO at T = 303 K.

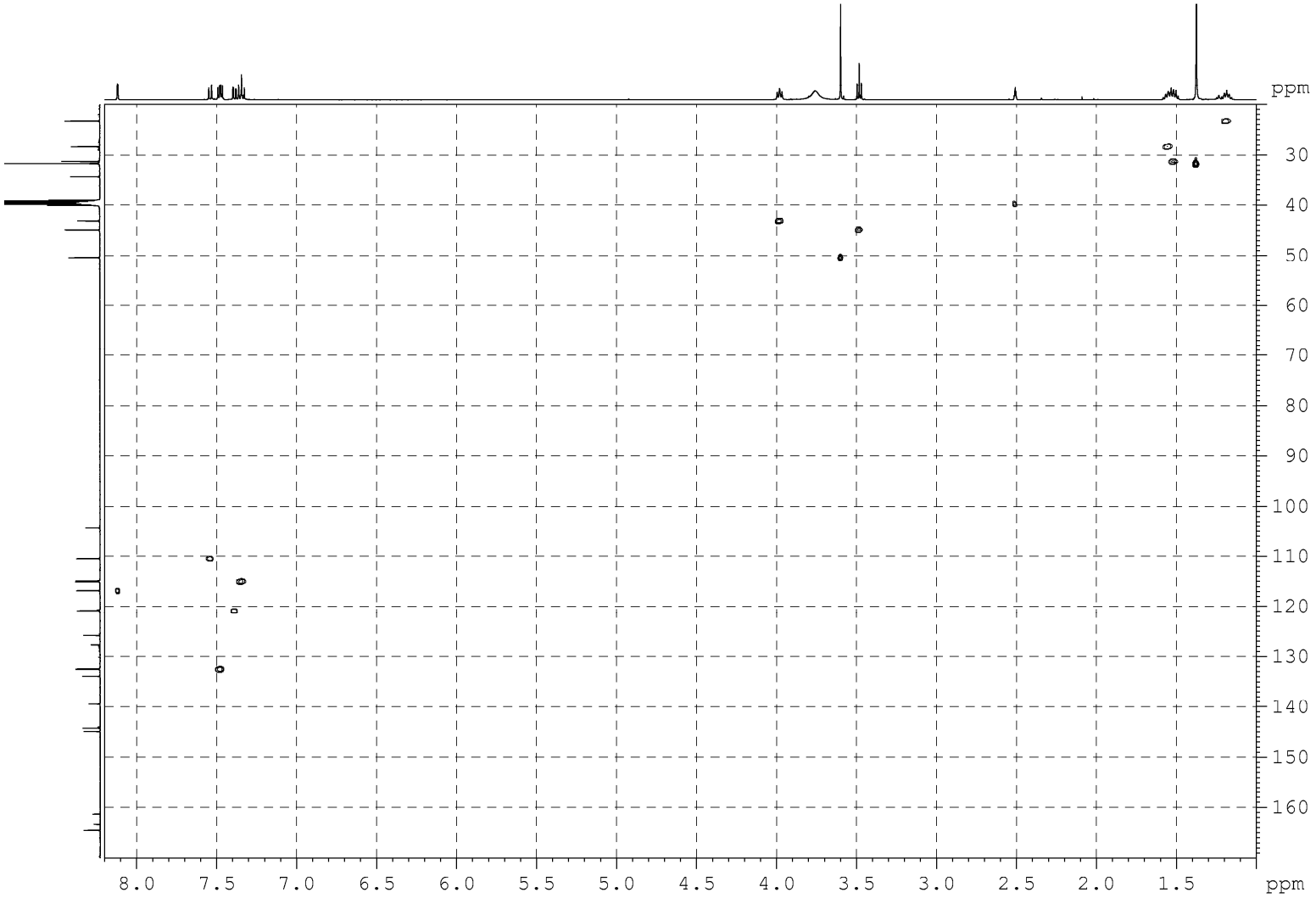

Figure S160. 2D ^{1}H-^{13}C HSQC NMR spectra of **11i** in DMSO at T = 303 K.

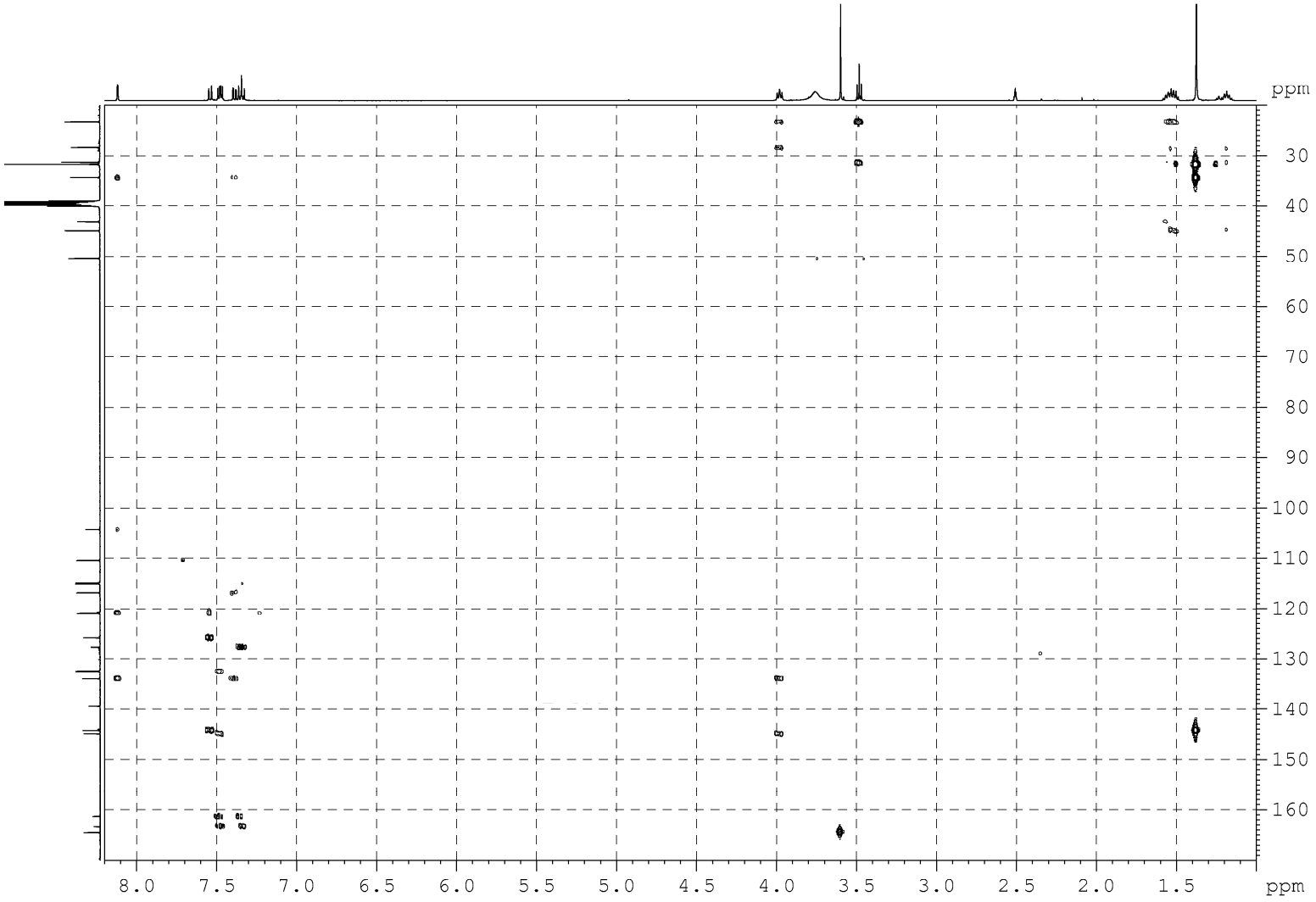

Figure S161. 2D ^{1}H-^{13}C HMBC NMR spectra of **11i** in DMSO at T = 303 K.

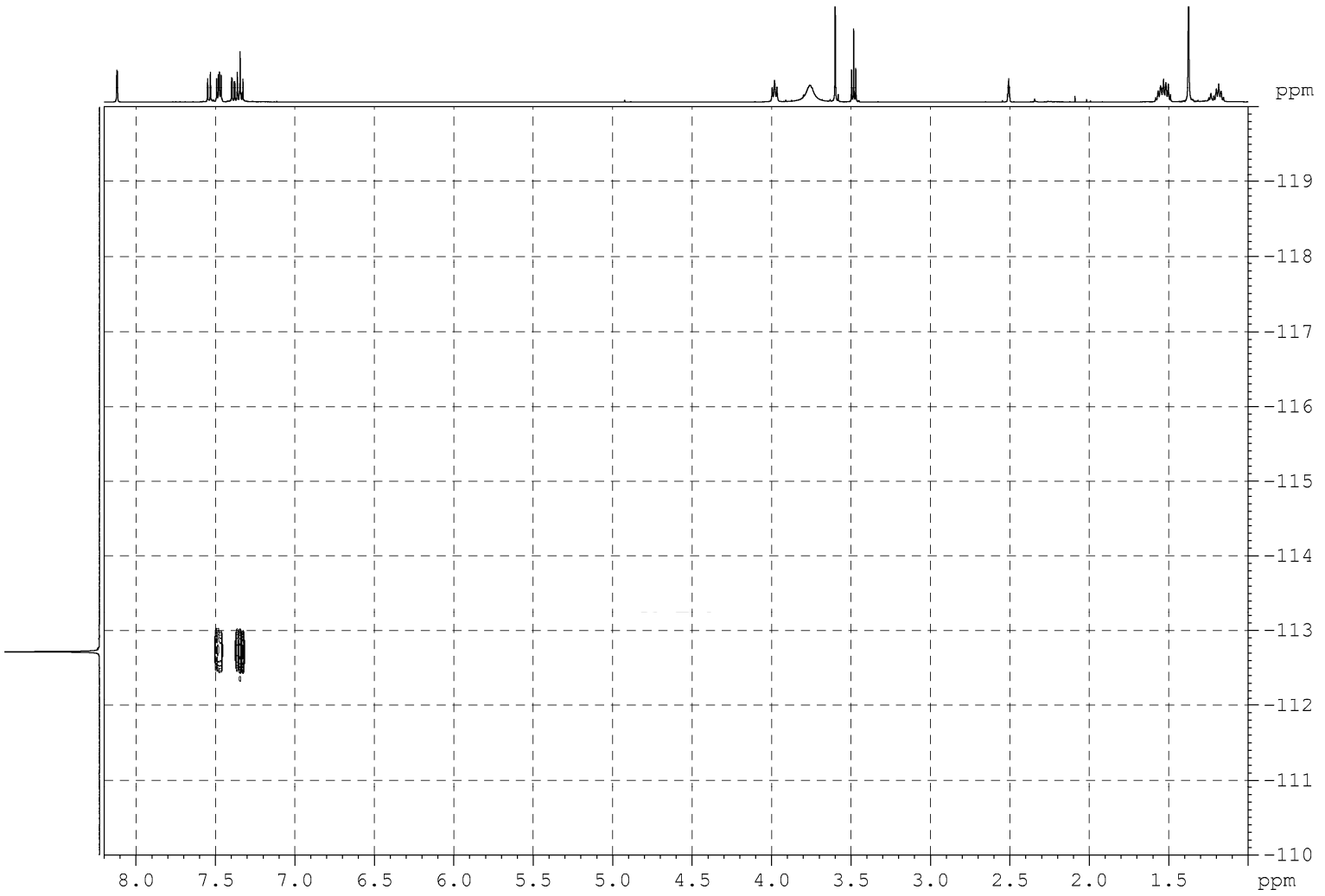

Figure S162. 2D ^{1}H-^{15}F HMBC NMR spectra of **11i** in DMSO at T = 303 K.

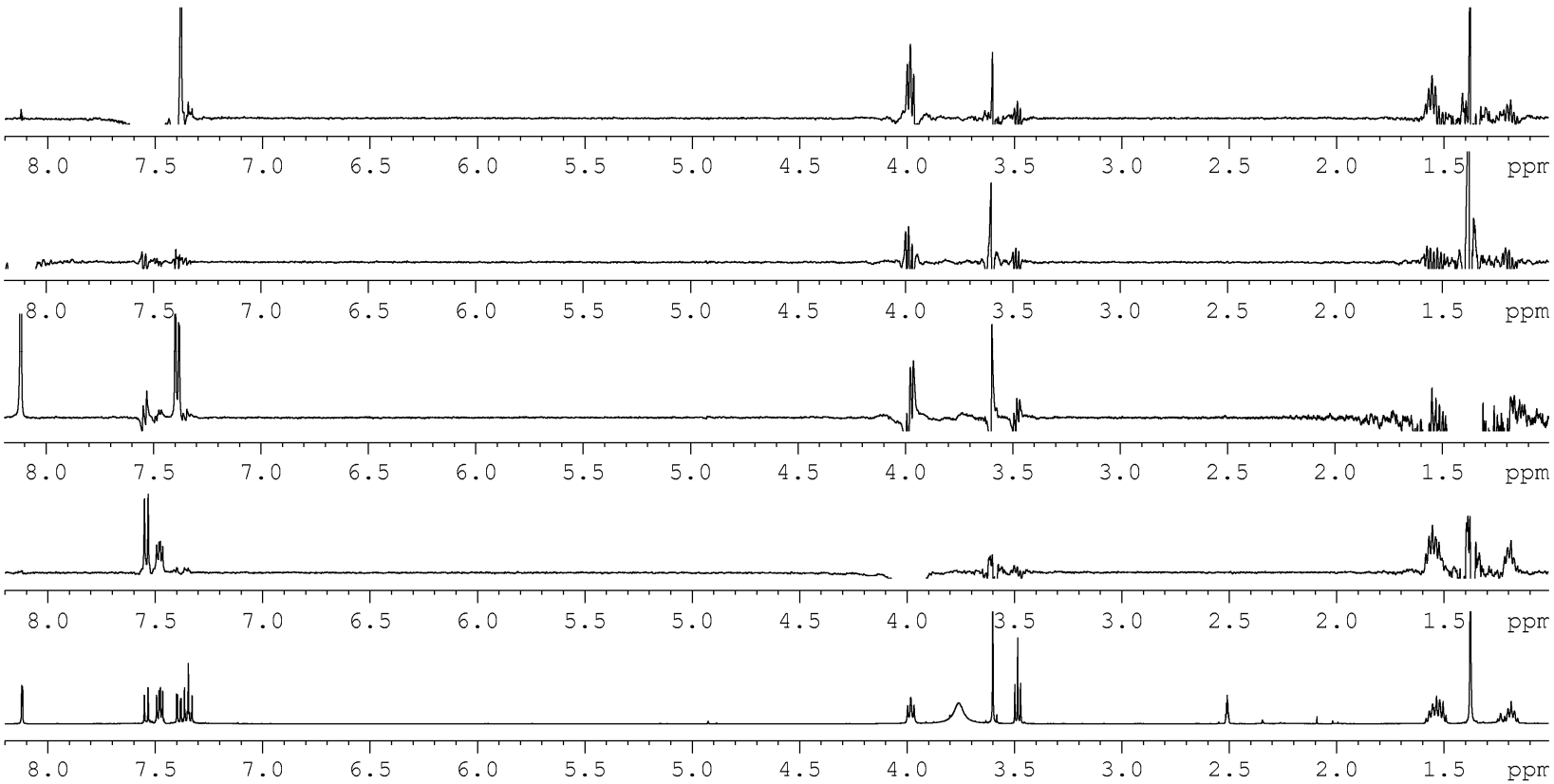

Figure S163. 1D ^{1}H and ^{1}H DPFGROE NMR spectra of **11i** in DMSO at T = 303 K.